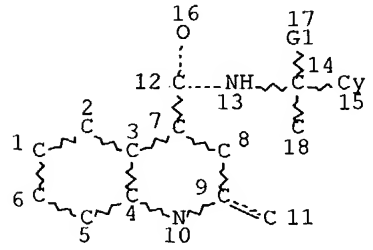
(FILE 'REGISTRY' ENTERED AT 10:26:35 ON 30 AUG 2004)

L1 STR



VAR G1=H/AK
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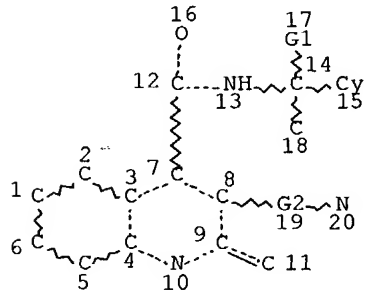
NSPEC IS RC AT 18
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE
L3 906 SEA FILE=REGISTRY SSS FUL L1
L13 STR



VAR G1=H/AK
REP G2=(1-10) CH2
NODE ATTRIBUTES:
NSPEC IS RC AT 11
NSPEC IS RC AT 18
NSPEC IS RC AT 20
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 20

STEREO ATTRIBUTES: NONE

L14 431 SEA FILE=REGISTRY SUB=L3 SSS FUL L13

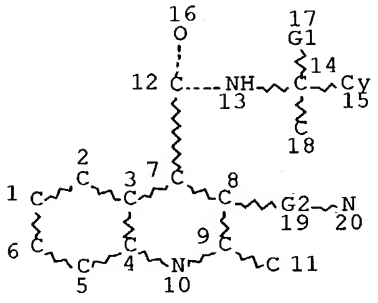
100.0% PROCESSED 432 ITERATIONS 431 ANSWERS
SEARCH TIME: 00.00.01

(FILE 'CAPLUS' ENTERED AT 10:29:25 ON 30 AUG 2004)
L15 19 S L14
L16 0 S L15 NOT (PY=>1997 OR PD=>19970523)

FILE 'CAOLD' ENTERED AT 10:35:19 ON 30 AUG 2004
L17 0 S L14

FILE 'USPATFULL' ENTERED AT 10:35:24 ON 30 AUG 2004
L18 16 S L14
L19 0 S L18 NOT (PY=>1997 OR PD=>19970523)

(FILE 'MARPAT' ENTERED AT 10:37:41 ON 30 AUG 2004)
L27 STR



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REP G2=(1-10) CH2
NODE ATTRIBUTES:
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NSPEC IS RC AT 18
NSPEC IS RC AT 20
DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 15 21
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

L29 11 SEA FILE=MARPAT SSS FUL L27 (MODIFIED ATTRIBUTES)

100.0% PROCESSED 16949 ITERATIONS 11 ANSWERS
SEARCH TIME: 00.01.17

L29 ANSWER 1 OF 11 MARPAT COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 137:337789 MARPAT Full-text
TITLE: Preparation of 3-(piperazinylalkyl)-4-quinolinecarboxamide derivatives as NK-3 and NK-2 receptor antagonists for treatment of respiratory diseases and CNS disorders
INVENTOR(S): Farina, Carlo; Gagliardi, Stefania; Giardina, Giuseppe Arnaldo Maria; Martinelli, Marisa
PATENT ASSIGNEE(S): Glaxosmithkline S.P.A., Italy
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002083664	A1	20021024	WO 2002-EP4070	20020411
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1385839	A1	20040204	EP 2002-761911	20020411
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004525184	T2	20040819	JP 2002-581419	20020411
PRIORITY APPLN. INFO.:			GB 2001-9123	20010411
			GB 2002-5649	20020311
			WO 2002-EP4070	20020411

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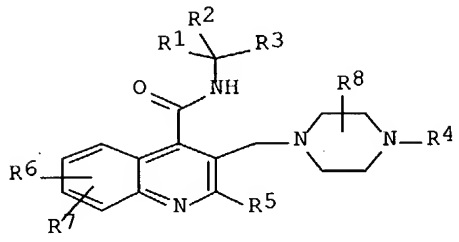

I

AB 3-Substituted quinoline-4-carboxamide derivs. [I; wherein R1 = H, alkyl; R2 = aryl, cycloalkyl, heteroaryl; R3 = H, alkyl, wherein the alkyl group may be optionally substituted by one or more fluorine atoms; R4 = H, hydroxyalkyl, dihydroxyalkyl, hydroxyalkoxyalkyl; R5 = branched or linear alkyl, cycloalkyl, cycloalkylalkyl, aryl, single or fused ring aromatic heterocyclic group; R6 = H, alkyl, alkenyl, aryl, alkoxy, hydroxy, halo, nitro, cyano, carboxy, carboxamido, sulfonamido, trifluoromethyl, amino,

mono- or di-alkylamino; R7 = H, halo; R8 = H, O] were prepared For example, 3-[4-(2-hydroxyethyl)-3-oxopiperazin-1-ylmethyl]-2-thiophen-2-ylquinoline- 4-carboxylic acid ((S)-1-cyclohexylethyl)amide was prepared by a multistep procedure. The prepared compds. were useful as nk-2 and nk-3 receptor antagonists.

IC ICM C07D401-06
ICS C07D409-14; C07D215-16; C07D215-52; A61K031-47; A61K031-4709; A61P011-00; A61P025-00; C07D401-06; C07D241-00; C07D215-00; C07D409-14; C07D333-00; C07D241-00; C07D215-00

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63

ST NK2 receptor antagonist prepn piperazinylalkyl quinolinecarboxamide deriv; NK3 receptor antagonist prepn piperazinylalkyl quinolinecarboxamide deriv; respiratory disease treatment piperazinylalkyl quinolinecarboxamide deriv prepn; CNS agent prepn piperazinylalkyl quinolinecarboxamide deriv prepn

IT AIDS (disease)
(AIDS dementia complex; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Mental disorder
(AIDS dementia; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Intestine, disease
(Crohn's; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Nervous system, disease
(Huntington's chorea; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Tachykinin receptors
(NK2 antagonists; preparation of quinoline carboxamide derivs. as)

IT Tachykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NK3 antagonists; preparation of quinoline carboxamide derivs. as)

IT Blood vessel, disease
(Raynaud's phenomenon; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Eye, disease
(allergic conjunctivitis; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Nervous system, disease
(amyotrophic lateral sclerosis; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Heart, disease
(angina pectoris; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Dermatitis
(atopic; preparation of piperazinylalkyl quinolinecarboxamides as NK-3

and
NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Lung, disease
(chronic obstructive; preparation of piperazinylalkyl quinolinecarboxamides
as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Eye, disease
(conjunctivitis; preparation of piperazinylalkyl quinolinecarboxamides as
NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Dermatitis
(contact; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and
NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Nervous system, disease
(degeneration; preparation of piperazinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Nerve, disease
(demyelination; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Mental disorder
(depression; preparation of piperazinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Nerve, disease
(diabetic neuropathy; preparation of piperazinylalkyl quinolinecarboxamides
as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Appetite
Blood coagulation
(disorder; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and
NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Blood pressure
(elevation; preparation of piperazinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Fasciola
(eosinophilic; preparation of piperazinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Digestive tract, disease
(gastroesophageal reflux; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Drugs

(gastrointestinal; preparation of piperazinylalkyl quinolinecarboxamides as
NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Respiratory tract, disease
(hyperresponsiveness; preparation of piperazinylalkyl quinolinecarboxamides
as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Bladder, disease
(incontinence; preparation of piperazinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Eye, disease
(inflammation; preparation of piperazinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Intestine, disease
Pain
(inflammatory; preparation of piperazinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Intestine, disease
(irritable bowel syndrome; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Headache
(migraine; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and
NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Nerve, disease
Pain
(neuralgia, chemotherapy-induced; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Inflammation
(neurogenic; preparation of piperazinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Nerve, disease
(neuropathy, AIDS-related or chemotherapy-induced; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Mental disorder
(neurotic depression; preparation of piperazinylalkyl quinolinecarboxamides
as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Nerve, disease
(peripheral neuropathy; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Alcoholism

Allergy
Allergy inhibitors
Alzheimer's disease
Analgesics
Anti-Alzheimer's agents
Anti-inflammatory agents
Antianginal agents
Antiarthritics
Antiasthmatics
Anticonvulsants
Antidepressants
Antihypertensives
Antimigraine agents
Antiparkinsonian agents
Antipsychotics
Antirheumatic agents
Anxiety
Anxiolytics
Asthma
Bladder, disease
Cardiovascular agents
Connective tissue, disease
Cough
Down's syndrome
Drug dependence
Drugs
Eczema
Epilepsy
Immunomodulators
Lupus erythematosus
Movement disorders
Multiple sclerosis
Nervous system agents
Osteoarthritis
Parkinson's disease
Preeclampsia
Pruritus
Psoriasis
Rheumatoid arthritis
Schizophrenia
Skin, disease
Stress, animal
Urticaria
(preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Human
(preparation of quinoline carboxamide derivs. as NK-3 and NK-2 receptor antagonists)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(proteinuria; preparation of piperazinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Mental disorder
(psychosis; preparation of piperazinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS

disorders)
IT Nervous system, disease
(reflex sympathetic dystrophy; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Nose, disease
(rhinitis; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and
NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Connective tissue, disease
(scleroderma; preparation of piperazinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Mental disorder
(senile psychosis; preparation of piperazinylalkyl quinolinecarboxamides as
NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Multiple sclerosis
(therapeutic agents; preparation of piperazinylalkyl quinolinecarboxamides
as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Intestine, disease
(ulcerative colitis; preparation of piperazinylalkyl quinolinecarboxamides
as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Skin, disease
(wheal-flare reaction; preparation of piperazinylalkyl quinolinecarboxamides
as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT 473298-89-4P 473552-69-1P 473552-70-4P 473552-71-5P 473552-72-6P
473552-73-7P 473552-74-8P 473552-75-9P 473552-76-0P 473552-77-1P
473552-78-2P 473552-79-3P 473552-80-6P 473552-81-7P 473552-82-8P
473552-83-9P 473552-84-0P 473552-85-1P 473552-86-2P 473552-87-3P
473552-88-4P 473552-89-5P 473552-90-8P 473552-91-9P 473552-92-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT 91-56-5, Isatine 93-55-0, Propiophenone 103-76-4, 1-Piperazineethanol
110-85-0, Piperazine, reactions 443-69-6 774-47-0, 5,6-Difluoroisatin
5317-32-8, 3-Piperazin-1-ylpropan-1-ol 5625-67-2, Piperazinone
13349-82-1 13679-75-9 17430-98-7, (S)-1-Cyclohexylethyl amine
17739-45-6 42330-88-1 42865-19-0, 2-Bromoethylisocyanate 51179-52-3
54533-84-5 57044-25-4 60456-23-7, (S)-(-)-Glycidol 76003-29-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT 31166-44-6P 43071-45-0P 270573-35-8P 425622-15-7P 425622-16-8P
425622-17-9P 433962-19-7P 433962-49-3P 433962-93-7P 433963-26-9P
473298-38-3P 473552-93-1P 473552-94-2P 473552-95-3P 473552-96-4P
473552-97-5P 473552-98-6P 473552-99-7P 473553-00-3P 473553-01-4P

473553-02-5P 473553-04-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 2 OF 11 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 137:310827 MARPAT Full-text
TITLE: Preparation of quinoline-4-carboxamide derivatives as NK3 and NK2 receptor antagonists
INVENTOR(S): Farina, Carlo; Gagliardi, Stefania; Giardina, Giuseppe Arnaldo Maria; Martinelli, Marisa
PATENT ASSIGNEE(S): Glaxosmithkline S.P.A., Italy
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002083663	A1	20021024	WO 2002-EP4066	20020411
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1377567	A1	20040107	EP 2002-735247	20020411
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004525183	T2	20040819	JP 2002-581418	20020411
US 2004152726	A1	20040805	US 2004-474542	20040315
PRIORITY APPLN. INFO.:			GB 2001-9123	20010411
			GB 2002-5649	20020311
			WO 2002-EP4066	20020411

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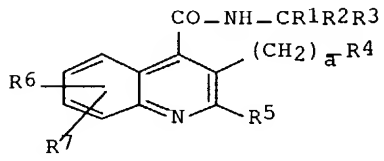

I

AB Disclosed are quinoline-4-carboxamide derivs. (shown as I; e.g. 6-fluoro-3-[3-oxo-4-(2-piperidin-1-ylethyl)piperazin-1-ylmethyl]-2- phenylquinoline-4-

carboxylic acid ((S)-1-cyclohexylethyl)amide), far more stable from a metabolic point of view than the known peptidic NK3 receptor antagonists, as detailed in the specification or a pharmaceutically acceptable salt or solvate thereof, a process for preparing such compds., a pharmaceutical composition comprising such compds. and the use of such compds. in medicine. In I: R1 is H or alkyl; R2 is aryl or cycloalkyl or heteroaryl; R3 is H or alkyl, wherein the group may be optionally substituted by ≥1 F atoms; R4 is NR8R9; R8 is H, alkyl or R11R12 and R9 is H, alkyl or R13R14; or R8 and R9 together with the N atom to which they are attached form a heterocyclic ring comprising 4-8 ring members, said ring members optionally including in addition to said N atom ≥1 further heteroatoms selected from N, O or S; and further detailed in the specification. Binding assays allowing the determination of the concentration of the individual compound required to reduce by 50% the [125I]-[Me-Phe7]-NKB and [3H]-Senktide specific binding to NK3 receptor in equilibrium conditions (IC50) show the most potent I have IC50 values of 0.1-1000 nM. Binding assays allowing the determination of the concentration of the individual compound required to reduce by 50% the [125I]-NKA and [3H]-NKA specific binding to NK2 receptor in equilibrium conditions (IC50) show the most potent I to have IC50 values of 0.5-1000 nM, such as 1-1000 nM. Example prepns. of about 16 intermediates and 35 I are included.

IC ICM C07D401-06
ICS C07D409-14; C07D215-16; A61K031-47; A61K031-4709; A61P011-00; A61P025-00; C07D417-06; C07D487-04; C07D401-06; C07D241-00; C07D215-00; C07D409-14; C07D333-00; C07D241-00; C07D215-00; C07D487-04; C07D241-00; C07D209-00

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

ST quinolinecarboxamide prepn NK2 NK3 receptor antagonist

IT AIDS (disease)
(AIDS dementia complex; preparation of quinolinecarboxamide derivs. as NK3 and NK2 receptor antagonists with various therapeutic uses)

IT Mental disorder
(AIDS dementia; preparation of quinolinecarboxamide derivs. as NK3 and NK2 receptor antagonists with various therapeutic uses)

IT Intestine, disease
(Crohn's; preparation of quinolinecarboxamide derivs. as NK3 and NK2 receptor antagonists with various therapeutic uses)

IT Nervous system, disease
(Huntington's chorea; preparation of quinolinecarboxamide derivs. as NK3 and NK2 receptor antagonists with various therapeutic uses)

IT Tachykinin receptors
(NK2 antagonists; preparation of quinolinecarboxamide derivs. as NK3 and NK2 receptor antagonists)

IT Blood vessel, disease
(Raynaud's phenomenon; preparation of quinolinecarboxamide derivs. as NK3 and NK2 receptor antagonists with various therapeutic uses)

IT Nervous system, disease
Nervous system agents
(amyotrophic lateral sclerosis; preparation of quinolinecarboxamide derivs. as NK3 and NK2 receptor antagonists with various therapeutic uses)

IT Heart, disease

(angina pectoris; preparation of quinolinecarboxamide derivs. as NK3 and NK2
receptor antagonists with various therapeutic uses)
IT Dermatitis
(atopic; preparation of quinolinecarboxamide derivs. as NK3 and NK2 receptor
antagonists with various therapeutic uses)
IT Lung, disease
(chronic obstructive; preparation of quinolinecarboxamide derivs. as NK3 and
NK2 receptor antagonists with various therapeutic uses)
IT Eye, disease
(conjunctivitis; preparation of quinolinecarboxamide derivs. as NK3 and NK2
receptor antagonists with various therapeutic uses)
IT Dermatitis
(contact; preparation of quinolinecarboxamide derivs. as NK3 and NK2
receptor antagonists with various therapeutic uses)
IT Nervous system, disease
(degeneration; preparation of quinolinecarboxamide derivs. as NK3 and NK2
receptor antagonists with various therapeutic uses)
IT Nerve, disease
(demyelination; preparation of quinolinecarboxamide derivs. as NK3 and NK2
receptor antagonists with various therapeutic uses)
IT Mental disorder
(depression; preparation of quinolinecarboxamide derivs. as NK3 and NK2
receptor antagonists with various therapeutic uses)
IT Nerve, disease
(diabetic neuropathy; preparation of quinolinecarboxamide derivs. as NK3 and
NK2 receptor antagonists with various therapeutic uses)
IT Appetite
Blood coagulation
(disorder; preparation of quinolinecarboxamide derivs. as NK3 and NK2
receptor antagonists with various therapeutic uses)
IT Brain, disease
(edema, following preeclampsia in pregnancies; preparation of
quinolinecarboxamide derivs. as NK3 and NK2 receptor antagonists with
various therapeutic uses)
IT Fasciola
(eosinophilic; preparation of quinolinecarboxamide derivs. as NK3 and NK2
receptor antagonists with various therapeutic uses)
IT Muscle, disease
(fibromyalgia; preparation of quinolinecarboxamide derivs. as NK3 and NK2
receptor antagonists with various therapeutic uses)
IT Lung, disease
(fibrosis; preparation of quinolinecarboxamide derivs. as NK3 and NK2
receptor antagonists with various therapeutic uses)
IT Digestive tract, disease
(gastroesophageal reflux; preparation of quinolinecarboxamide derivs. as NK3
and NK2 receptor antagonists with various therapeutic uses)
IT Respiratory tract, disease
(hyperresponsiveness; preparation of quinolinecarboxamide derivs. as NK3

and
NK2 receptor antagonists with various therapeutic uses)
IT Bladder, disease
(incontinence; preparation of quinolinecarboxamide derivs. as NK3 and NK2
receptor antagonists with various therapeutic uses)
IT Eye, disease
(inflammation; preparation of quinolinecarboxamide derivs. as NK3 and NK2
receptor antagonists with various therapeutic uses)
IT Intestine, disease
Pain
(inflammatory; preparation of quinolinecarboxamide derivs. as NK3 and NK2
receptor antagonists with various therapeutic uses)
IT Intestine, disease
(irritable bowel syndrome; preparation of quinolinecarboxamide derivs. as
NK3 and NK2 receptor antagonists with various therapeutic uses)
IT Headache
(migraine; preparation of quinolinecarboxamide derivs. as NK3 and NK2
receptor antagonists with various therapeutic uses)
IT Nerve, disease
Pain
(neuralgia; preparation of quinolinecarboxamide derivs. as NK3 and NK2
receptor antagonists with various therapeutic uses)
IT Inflammation
(neurogenic; preparation of quinolinecarboxamide derivs. as NK3 and NK2
receptor antagonists with various therapeutic uses)
IT Nerve, disease
(neuropathy, AIDs-related and chemotherapy-induced; preparation of
quinolinecarboxamide derivs. as NK3 and NK2 receptor antagonists with
various therapeutic uses)
IT Mental disorder
(neurotic depression; preparation of quinolinecarboxamide derivs. as NK3 and
NK2 receptor antagonists with various therapeutic uses)
IT Nerve, disease
(peripheral neuropathy; preparation of quinolinecarboxamide derivs. as NK3
and NK2 receptor antagonists with various therapeutic uses)
IT Alcoholism
Allergy
Allergy inhibitors
Alzheimer's disease
Analgesics
Anti-Alzheimer's agents
Anti-inflammatory agents
Antianginal agents
Antiarthritics
Antiasthmatics
Anticonvulsants
Antidepressants
Antihypertensives
Antimigraine agents
Antiparkinsonian agents
Antipsychotics
Antirheumatic agents

Anxiety
Anxiolytics
Asthma
Bladder, disease
Connective tissue, disease
Cough
Digestive tract, disease
Down's syndrome
Drug dependence
Eczema
Epilepsy
Eye, disease
Human
Hypertension
Inflammation
Kidney, disease
Movement disorders
Multiple sclerosis
Nervous system agents
Osteoarthritis
Parkinson's disease
Psoriasis
Respiratory tract, disease
Rheumatoid arthritis
Schizophrenia
Skin, disease
Stress, animal
Transplant rejection
Urticaria
Vasodilation
(preparation of quinolinecarboxamide derivs. as NK3 and NK2 receptor antagonists with various therapeutic uses)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(proteinuria; preparation of quinolinecarboxamide derivs. as NK3 and NK2 receptor antagonists with various therapeutic uses)

IT Mental disorder
(psychosis; preparation of quinolinecarboxamide derivs. as NK3 and NK2 receptor antagonists with various therapeutic uses)

IT Nervous system, disease
(reflex sympathetic dystrophy; preparation of quinolinecarboxamide derivs.
as NK3 and NK2 receptor antagonists with various therapeutic uses)

IT Nose, disease
(rhinitis; preparation of quinolinecarboxamide derivs. as NK3 and NK2 receptor antagonists with various therapeutic uses)

IT Connective tissue, disease
(scleroderma; preparation of quinolinecarboxamide derivs. as NK3 and NK2 receptor antagonists with various therapeutic uses)

IT Mental disorder
(senile psychosis; preparation of quinolinecarboxamide derivs. as NK3 and
NK2 receptor antagonists with various therapeutic uses)

IT Lupus erythematosus
(systemic; preparation of quinolinecarboxamide derivs. as NK3 and NK2 receptor antagonists with various therapeutic uses)

IT Multiple sclerosis
(therapeutic agents; preparation of quinolinecarboxamide derivs. as NK3

and
NK2 receptor antagonists with various therapeutic uses)
IT Tachykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type NK3, antagonists; preparation of quinolinecarboxamide derivs. as NK3
and NK2 receptor antagonists)
IT Intestine, disease
(ulcerative colitis; preparation of quinolinecarboxamide derivs. as NK3
and NK2 receptor antagonists with various therapeutic uses)
IT Skin, disease
(wheal-flare reaction; preparation of quinolinecarboxamide derivs. as NK3
and NK2 receptor antagonists with various therapeutic uses)
IT 473298-42-9P, 6-Fluoro-3-[[3-oxo-4-(2-(piperidin-1-yl)ethyl)piperazin-1-yl]methyl]-2-phenylquinoline-4-carboxylic acid ((S)-1-cyclohexylethyl)amide 473298-43-0P 473298-44-1P, 3-[(1-Oxo-3,4-dihydro-1H-pyrrolo[1,2-a]pyrazin-2-yl)methyl]-2-phenylquinoline-4-carboxylic acid ((S)-1-cyclohexylethyl)amide 473298-45-2P, 3-Dimethylaminomethyl-6-fluoro-2-phenylquinoline-4-carboxylic acid ((S)-1-cyclohexylethyl)amide 473298-46-3P, 6-Fluoro-3-[(1-oxo-3,4-dihydro-1H-pyrrolo[1,2-a]pyrazin-2-yl)methyl]-2-phenylquinoline-4-carboxylic acid ((S)-1-cyclohexylethyl)amide 473298-47-4P, 3-[[4-(3-Dimethylaminopropyl)-3-oxopiperazin-1-yl]methyl]-2-phenylquinoline-4-carboxylic acid ((S)-1-cyclohexylethyl)amide 473298-49-6P, 3-[(4-Methyl-3-oxopiperazin-1-yl)methyl]-2-phenylquinoline-4-carboxylic acid ((S)-1-cyclohexylethyl)amide bis trifluoroacetate 473298-50-9P, 3-[(4-Ethyl-3-oxopiperazin-1-yl)methyl]-2-phenylquinoline-4-carboxylic acid ((S)-1-cyclohexylethyl)amide 473298-51-0P, 3-[(2-Oxoimidazolidin-1-yl)methyl]-2-phenylquinoline-4-carboxylic acid ((S)-1-cyclohexylethyl)amide 473298-52-1P, 3-[[3-Oxo-4-(2-(pyrrolidin-1-yl)ethyl)piperazin-1-yl]methyl]-2-phenylquinoline-4-carboxylic acid ((S)-1-cyclohexylethyl)amide 473298-53-2P, 3-[[4-(2-Diethylaminoethyl)-3-oxopiperazin-1-yl]methyl]-2-phenylquinoline-4-carboxylic acid ((S)-1-cyclohexylethyl)amide 473298-54-3P, 3-[[4-(2-Dimethylaminoethyl)-3-oxopiperazin-1-yl]methyl]-2-phenylquinoline-4-carboxylic acid ((S)-1-cyclohexylethyl)amide 473298-55-4P, 3-[[4-(2-Aminoethyl)-3-oxopiperazin-1-yl]methyl]-2-phenylquinoline-4-carboxylic acid ((S)-1-cyclohexylethyl)amide 473298-57-6P, 3-[[4-(2-(Morpholin-4-yl)ethyl)-3-oxopiperazin-1-yl]methyl]-2-phenylquinoline-4-carboxylic acid ((S)-1-cyclohexylethyl)amide 473298-58-7P, 3-[(4-Ethylcarbamoylpiperazin-1-yl)methyl]-2-phenylquinoline-4-carboxylic acid ((S)-1-cyclohexylethyl)amide 473298-59-8P, 3-[(4-Isopropylcarbamoylpiperazin-1-yl)methyl]-2-phenylquinoline-4-carboxylic acid ((S)-1-cyclohexylethyl)amide 473298-60-1P, 3-[(3-Oxopiperazin-1-yl)methyl]-2-(thiophen-3-yl)quinoline-4-carboxylic acid ((S)-1-cyclohexylethyl)amide 473298-61-2P, 3-[[4-(3-Dimethylaminopropyl)-3-oxopiperazin-1-yl]methyl]-6-fluoro-2-phenylquinoline-4-carboxylic acid ((S)-1-cyclohexylethyl)amide 473298-62-3P, N-((S)-1-Cyclohexylethyl)-3-(((3-(diethylamino)propyl)(methyl)amino)methyl)-2-phenylquinoline-4-carboxamide 473298-63-4P, N-((S)-1-Cyclohexylethyl)-3-((hexahydro-1H-1,4-diazepin-1-yl)methyl)-2-phenylquinoline-4-carboxamide 473298-64-5P, N-((S)-1-Cyclohexylethyl)-3-((dipropylamino)methyl)-2-phenylquinoline-4-carboxamide 473298-65-6P, N-((S)-1-Cyclohexylethyl)-3-(((1-benzyl-4-piperidino)amino)methyl)-2-phenylquinoline-4-carboxamide 473298-66-7P, N-((S)-1-Cyclohexylethyl)-3-(((2-indanyl)amino)methyl)-2-phenylquinoline-4-carboxamide 473298-68-9P, N-((S)-1-Cyclohexylethyl)-3-((thiazolidin-3-

yl)methyl)-2-phenylquinoline-4-carboxamide 473298-71-4P, N-((S)-1-Cyclohexylethyl)-3-(((benzyl)(2-hydroxyethyl)amino)methyl)-2-phenylquinoline-4-carboxamide 473298-72-5P, N-((S)-1-Cyclohexylethyl)-3-((2,3-dihydro-1H-indol-1-yl)methyl)-2-phenylquinoline-4-carboxamide 473298-73-6P, N-((S)-1-Cyclohexylethyl)-3-((butylamino)methyl)-2-phenylquinoline-4-carboxamide 473298-75-8P, N-((S)-1-Cyclohexylethyl)-3-(((R)-3-hydroxypyrrolidin-1-yl)methyl)-2-phenylquinoline-4-carboxamide 473298-77-0P, N-((S)-1-Cyclohexylethyl)-3-((dimethylamino)methyl)-2-phenylquinoline-4-carboxamide 473298-79-2P, N-((S)-1-Cyclohexylethyl)-3-(((S)-3-hydroxypyrrolidin-1-yl)methyl)-2-phenylquinoline-4-carboxamide 473298-81-6P, N-((S)-1-Cyclohexylethyl)-3-((1,2,3,4-tetrahydro-2-isoquinolinyl)methyl)-2-phenylquinoline-4-carboxamide 473298-83-8P, N-((S)-1-Cyclohexylethyl)-3-(((methyl)(2,2,6,6-tetramethyl-4-piperidino)amino)methyl)-2-phenylquinoline-4-carboxamide 473298-85-0P, N-((S)-1-Cyclohexylethyl)-3-((4-oxopiperidino)methyl)-2-phenylquinoline-4-carboxamide 473298-87-2P, 3-[(3,4-Dihydro-1H-pyrrolo[1,2-a]pyrazin-2-yl)methyl]-2-phenylquinoline-4-carboxylic acid ((S)-1-cyclohexylethyl)amide 473298-88-3P 473298-89-4P, N-((S)-1-Cyclohexylethyl)-3-((4-(((2-hydroxyethyl)amino)carbonyl)-1-piperazino)methyl)-2-phenylquinoline-4-carboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of quinoline-4-carboxamide derivs. as NK3 and NK2 receptor antagonists)

IT 43071-45-0P, 3-Methyl-2-phenylquinoline-4-carboxylic acid 57260-71-6P 270573-35-8P, 2-Phenyl-3-(piperazin-1-yl)methylquinoline-4-carboxylic acid ((S)-1-cyclohexylethyl)amide 425622-15-7P, N-((S)-1-Cyclohexylethyl)-3-methyl-2-phenylquinoline-4-carboxamide 425622-16-8P 425622-17-9P, 4-[[4-((S)-1-Cyclohexylethylcarbamoyl)-2-phenylquinolin-3-yl]methyl]piperazine-1-carboxylic acid tert-butyl ester 433962-19-7P, 3-[(3-Oxopiperazin-1-yl)methyl]-2-phenylquinoline-4-carboxylic acid ((S)-1-cyclohexylethyl)amide 433962-93-7P, 3-Bromomethyl-6-fluoro-2-phenylquinoline-4-carboxylic acid ((S)-1-cyclohexylethyl)amide 473298-38-3P, 6,7-Difluoro-3-methyl-2-phenylquinoline-4-carboxylic acid 473298-41-8P, 4-[[4-((S)-1-Cyclohexylethylcarbamoyl)-6-fluoro-2-phenylquinolin-3-yl]methyl]-3-oxopiperazine-1-carboxylic acid tert-butyl ester 473298-56-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of quinoline-4-carboxamide derivs. as NK3 and NK2 receptor antagonists)

IT 91-56-5, Isatine 93-55-0, Propiophenone 100-35-6, 2-Diethylaminoethyl chloride 107-99-3, 2-(Dimethylamino)ethyl chloride 109-54-6, 3-Dimethylaminopropyl chloride 109-90-0, Ethyl isocyanate 110-85-0, Piperazine, reactions 120-93-4, 2-Imidazolidone 443-69-6, 5-Fluoroisatine 774-47-0, 5,6-Difluoroisatine 1458-63-5, 1-(3-Chloropropyl)piperidine 1795-48-8, Isopropyl isocyanate 1932-03-2, 1-(2-Chloroethyl)piperidine 3240-94-6, 4-(2-Chloroethyl)morpholine 5050-41-9, 1-(2-Chloroethyl)pyrrolidine 5625-67-2, Piperazin-2-one 13679-75-9, 1-(Thiophen-2-yl)propan-1-one 17430-98-7, (S)-1-Cyclohexylethylamine 39684-80-5, 2-(tert-Butyloxycarbonylamino)ethyl bromide 51179-52-3, 1-(Thiophen-3-yl)propan-1-one 54906-42-2, 3,4-Dihydro-2H-pyrrolo[1,2-a]pyrazin-1-one 76003-29-7, 3-Oxopiperazine-1-carboxylic acid tert-butyl ester
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of quinoline-4-carboxamide derivs. as NK3 and NK2 receptor antagonists)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 3 OF 11 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 137:310826 MARPAT Full-text
TITLE: Preparation of quinoline derivatives as NK3 and NK2 receptor antagonists
INVENTOR(S): Farina, Carlo; Giardina, Giuseppe Arnaldo Maria; Grugni, Mario; Perugini, Lorenzo
PATENT ASSIGNEE(S): Glaxosmithkline S.P.A., Italy
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002083645	A1	20021024	WO 2002-EP4069	20020411
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1377555	A1	20040107	EP 2002-730147	20020411
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004152730	A1	20040805	US 2004-474556	20040315
PRIORITY APPLN. INFO.:			GB 2001-9122	20010411
			WO 2002-EP4069	20020411

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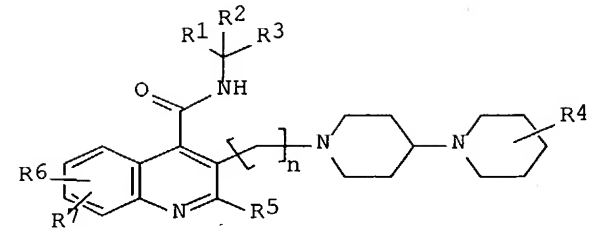

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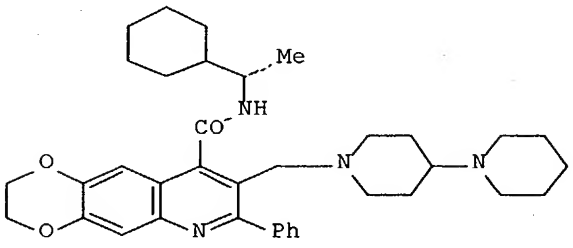

II

AB Quinoline derivs. of formula I [R1 = H, alkyl; R2 = arylalkyl, etc.; R3 = H, alkyl, cycloalkyl; R4 = H, F; R5 = alkyl, cycloalkyl, aryl, aryl; R6 = H, alkyl, aryl, alkoxy, OH, halo, CN, etc.; R7 = H, alkoxy, halo; R6R7 = alkylenedioxy; n = 1-6] are prepared as NK3 and NK2 receptor antagonists. Thus, II was prepared in several steps. The most potent compds. had IC50 values of 0.1-1000 nM in binding assays on NK3 receptors.

IC ICM C07D215-52
ICS C07D401-14; A61K031-47; C07D405-14

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

ST quinoline deriv prepn NK3 receptor antagonist; NK2 receptor antagonist quinoline deriv prepn

IT Tachykinin receptors
(NK2 antagonists; preparation of quinoline derivs. as NK3 and NK2 receptor antagonists)

IT Immunity
(disorder; preparation of quinoline derivs. as NK3 and NK2 receptor antagonists)

IT Digestive tract, disease
Eye, disease
Human
Hypertension
Inflammation
Kidney, disease
Respiratory tract, disease
Skin, disease
Urinary tract, disease
(preparation of quinoline derivs. as NK3 and NK2 receptor antagonists)

IT Tachykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type NK3, antagonists; preparation of quinoline derivs. as NK3 and NK2 receptor antagonists)

IT 473248-13-4P 473248-14-5P 473248-15-6P 473248-16-7P 473248-17-8P
473248-18-9P 473248-19-0P 473248-20-3P 473248-21-4P 473248-22-5P
473248-23-6P 473248-24-7P 473248-25-8P 473248-26-9P 473248-27-0P

473248-28-1P 473248-29-2P 473248-30-5P 473248-31-6P 473248-32-7P
473248-33-8P 473248-34-9P 473248-35-0P 473248-36-1P 473248-37-2P
473248-38-3P 473248-39-4P 473248-40-7P 473248-41-8P 473248-42-9P
473248-43-0P 473248-44-1P 473248-45-2P 473248-46-3P 473248-47-4P
473248-48-5P 473248-49-6P 473248-50-9P 473248-51-0P 473248-52-1P
473248-53-2P 473248-54-3P 473248-55-4P 473248-56-5P 473248-57-6P
473248-58-7P 473248-59-8P 473248-60-1P 473248-61-2P 473248-62-3P
473248-63-4P 473248-64-5P 473248-65-6P 473248-66-7P 473248-67-8P
473248-69-0P 473248-70-3P 473248-71-4P 473248-72-5P 473248-73-6P
473248-74-7P 473248-75-8P 473248-76-9P 473248-77-0P 473248-78-1P
473248-79-2P 473248-80-5P 473248-81-6P 473248-82-7P 473248-83-8P
473248-84-9P 473248-85-0P 473248-86-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinoline derivs. as NK3 and NK2 receptor antagonists)

IT 91-56-5, Isatin 99-05-8, m-Aminobenzoic acid 100-52-7, Benzaldehyde, reactions 600-18-0, 2-Oxobutyric acid 1011-62-7, 5-Hydroxy-1-phenylpentan-1-one 4897-50-1, 4-Piperidinopiperidine 14268-66-7, 3,4-Methylenedioxyaniline 17430-98-7 21120-36-5, 2-Fluoropropiophenone 22013-33-8, 1,4-Benzodioxan-6-amine 43071-45-0 473248-97-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of quinoline derivs. as NK3 and NK2 receptor antagonists)

IT 1877-77-6P 74960-43-3P 154869-08-6P 270574-03-3P 272104-64-0P
433962-68-6P 433963-02-1P 473248-87-2P 473248-88-3P 473248-89-4P
473248-90-7P 473248-91-8P 473248-93-0P 473248-95-2P 473248-99-6P
473249-01-3P 473249-02-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of quinoline derivs. as NK3 and NK2 receptor antagonists)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 4 OF 11 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 137:20387 MARPAT Full-text
TITLE: Preparation of 3-(piperazinylalkyl)-4-quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders
INVENTOR(S): Farina, Carlo; Gagliardi, Stefania; Giardina, Giuseppe; Grugni, Mario; Nadler, Guy Marguerite Marie Gerard; Martinelli, Marisa
PATENT ASSIGNEE(S): Glaxosmithkline S.P.A., Italy; Laboratoire Glaxosmithkline S.A.S.
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002044165	A1	20020606	WO 2001-EP13833	20011126

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA,

UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002026356	A5	20020611	AU 2002-26356	20011126
EP 1351953	A1	20031015	EP 2001-995670	20011126
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004517082	T2	20040610	JP 2002-546535	20011126
US 2004097518	A1	20040520	US 2003-432925	20031124
PRIORITY APPLN. INFO.:			GB 2000-28965	20001128
			GB 2001-9118	20010411
			WO 2001-EP13833	20011126

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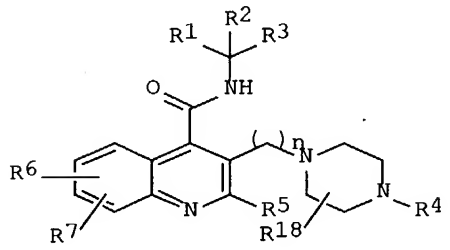

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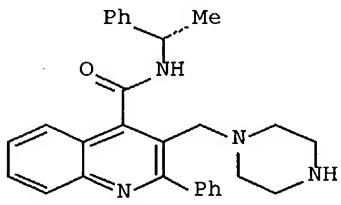

II

AB Title compds. I [wherein R1 = H or alkyl; R2 = (un)substituted (hetero)aryl or cycloalkyl; R3 = H, alkyl, or cycloalkyl(alkyl) (un)substituted by 1 or more fluorines; R4 = H or R8R9; R5 = branched or linear alkyl, cycloalkyl(alkyl), aryl, or single or fused-ring aromatic (un)substituted heterocyclic group; R6 = H, or 1-3 of alkyl, alkenyl, aryl, alkoxy, OH, halo, NO2, cyano, CO2H, alkylcarboxy(alkyl), haloalkyl, NH2, or (di)(alkyl)amino; or R6 = a bridging alkyl or dioxyalkylene; R7 = H or halo; R8 = (un)substituted alkyl or alkenyl; R9 = S(O2)R10, S(O2)OR10, ONO, CO2R10, CONR11R12, or CN; R10 = H, (cyclo)alkyl, or aryl; R11 and R12 = independently H or alkyl; R18 = H or up to 3 oxo groups; any of R2, R5, R8, R10, R11, or R12 may be (un)substituted 1 or more times by halo, OH, NH2, cyano, NO2, CO2H, or oxo; n = 1-6; with 26 compds. excluded; and their pharmaceutically acceptable salts or hydrates] were prepared I are a novel class of potent non-peptide neurokinin-3 (NK-3) antagonists, some of which fall within the generic scope of WO 00/31037. I are far more stable metabolically and show improved oral bioavailability compared to the known peptidic NK-3 receptor antagonists (no data). In addition, I have good NK-2 antagonist activity and are considered to be of potential use in the

prevention and treatment of a wide variety of clin. conditions which are characterized by over-stimulation of tachykinin receptors, in particular NK-3 and NK-2. Forty-eight specific (S)-isomeric compds. I were prepared For instance, 4-carboxy-3-methyl-2-phenylquinoline was subjected to the sequence of (1) Me esterification; (2) α-bromination; (3) amination of the bromide with piperazine-1-carboxylic acid tert-Bu ester; (4) ester hydrolysis (95%); and (5) amidation with (S)-1-phenylethylamine to give the title compound II. In binding assays using human NK-2 receptors and guinea pig and human NK-3 receptors, the most potent I exhibited IC50 values ranging from 0.5 nM to 1000 nM and from 0.1 nM to 1000 nM, resp.

IC ICM C07D401-06
ICS A61K031-495; A61P025-00; A61P029-00

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

ST piperazinylalkyl quinolinecarboxamide prepn neurokinin receptor antagonist; NK2 NK3 receptor antagonist quinolinecarboxamide CNS agent; NK3 NK2 receptor antagonist quinolinecarboxamide respiratory disease treatment

IT AIDS (disease)
(AIDS dementia complex; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Mental disorder
(AIDS dementia; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Intestine, disease
(Crohn's; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Nervous system, disease
(Huntington's chorea; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Tachykinin receptors
(NK2 antagonists; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Tachykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NK3 antagonists; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Blood vessel, disease
(Raynaud's phenomenon; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Eye, disease
(allergic conjunctivitis; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Nervous system, disease
(amyotrophic lateral sclerosis; preparation of piperazinylalkyl

quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Heart, disease
(angina pectoris; preparation of piperazinylalkyl quinolinecarboxamides as
NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Dermatitis
(atopic; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and
NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Lung, disease
(chronic obstructive; preparation of piperazinylalkyl quinolinecarboxamides
as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Eye, disease
(conjunctivitis; preparation of piperazinylalkyl quinolinecarboxamides as
NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Dermatitis
(contact; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and
NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Nervous system, disease
(degeneration; preparation of piperazinylalkyl quinolinecarboxamides as
NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Nerve, disease
(demyelination; preparation of piperazinylalkyl quinolinecarboxamides as
NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Mental disorder
(depression; preparation of piperazinylalkyl quinolinecarboxamides as
NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Nerve, disease
(diabetic neuropathy; preparation of piperazinylalkyl quinolinecarboxamides
as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Appetite
Blood coagulation
(disorder; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and
NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Blood pressure
(elevation; preparation of piperazinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Fasciola

(eosinophilic; preparation of piperazinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Digestive tract, disease
(gastroesophageal reflux; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Drugs
(gastrointestinal; preparation of piperazinylalkyl quinolinecarboxamides as
NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Respiratory tract, disease
(hyperresponsiveness; preparation of piperazinylalkyl quinolinecarboxamides
as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Bladder, disease
(incontinence; preparation of piperazinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Eye, disease
(inflammation; preparation of piperazinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Intestine, disease
Pain
(inflammatory; preparation of piperazinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Intestine, disease
(irritable bowel syndrome; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Headache
(migraine; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and
NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Nerve, disease
Pain
(neuralgia, chemotherapy-induced; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Inflammation
(neurogenic; preparation of piperazinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Nerve, disease
(neuropathy, AIDS-related or chemotherapy-induced; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Mental disorder

(neurotic depression; preparation of piperazinylalkyl quinolinecarboxamides
as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Nerve, disease
(peripheral neuropathy; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Alcoholism
Allergy
Allergy inhibitors
Alzheimer's disease
Analgesics
Anti-Alzheimer's agents
Anti-inflammatory agents
Antianginal agents
Antiarthritics
Antiasthmatics
Anticonvulsants
Antidepressants
Antihypertensives
Antimigraine agents
Antiparkinsonian agents
Antipsychotics
Antirheumatic agents
Anxiety
Anxiolytics
Asthma
Bladder, disease
Cardiovascular agents
Connective tissue, disease
Cough
Down's syndrome
Drug dependence
Drugs
Eczema
Epilepsy
Human
Immunomodulators
Lupus erythematosus
Movement disorders
Multiple sclerosis
Nervous system agents
Osteoarthritis
Parkinson's disease
Preeclampsia
Pruritus
Psoriasis
Rheumatoid arthritis
Schizophrenia
Skin, disease
Stress, animal
Urticaria
(preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(proteinuria; preparation of piperazinylalkyl quinolinecarboxamides as

NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Mental disorder
(psychosis; preparation of piperazinylalkyl quinolinecarboxamides as NK-3
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(reflex sympathetic dystrophy; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Nose, disease
(rhinitis; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and
NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Connective tissue, disease
(scleroderma; preparation of piperazinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Mental disorder
(senile psychosis; preparation of piperazinylalkyl quinolinecarboxamides as
NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Multiple sclerosis
(therapeutic agents; preparation of piperazinylalkyl quinolinecarboxamides
as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Tachykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type NK2; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and
NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Tachykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type NK3; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and
NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Intestine, disease
(ulcerative colitis; preparation of piperazinylalkyl quinolinecarboxamides
as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Skin, disease
(wheal-flare reaction; preparation of piperazinylalkyl quinolinecarboxamides
as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT 425622-13-5P 433961-77-4P 433961-80-9P 433962-06-2P 433962-19-7P
433962-21-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); RACT (Reactant or reagent); USES (Uses)
(NT-2 and NT-3 receptor antagonist; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT 433961-76-3P 433961-79-6P 433961-81-0P 433961-82-1P 433961-84-3P
433961-85-4P 433961-86-5P 433961-87-6P 433961-88-7P 433961-90-1P
433961-92-3P 433961-94-5P 433961-97-8P 433962-00-6P 433962-02-8P
433962-04-0P 433962-09-5P 433962-11-9P 433962-13-1P 433962-15-3P
433962-17-5P 433962-23-3P 433962-25-5P 433962-28-8P 433962-30-2P
433962-32-4P 433962-34-6P 433962-36-8P 433962-38-0P 433962-40-4P
433962-42-6P 433962-44-8P 433962-47-1P 433962-49-3P 433962-51-7P
433962-53-9P 433962-55-1P 433962-57-3P 433962-59-5P 433962-61-9P
433962-63-1P 433967-86-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(NT-2 and NT-3 receptor antagonist; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT 43071-45-0P 57260-71-6P 74960-43-3P, 3-Methyl-2-phenylquinoline-4-carboxylic acid methyl ester 130507-38-9P, 6-Fluoro-3-methyl-2-phenylquinoline-4-carboxylic acid 154869-08-6P, 7-Methyl-6-phenyl-[1,3]dioxolo[4,5-g]quinoline-8-carboxylic acid 270574-10-2P
270574-11-3P 270574-13-5P 270574-14-6P 270574-15-7P 425622-12-4P
433962-65-3P, 3-(4-tert-Butoxycarbonylpiperazin-1-ylmethyl)-2-phenylquinoline-4-carboxylic acid methyl ester 433962-67-5P,
3-(4-tert-Butoxycarbonylpiperazin-1-ylmethyl)-2-phenylquinoline-4-carboxylic acid 433962-68-6P 433962-70-0P 433962-81-3P
433962-83-5P 433962-85-7P 433962-87-9P 433962-89-1P 433962-91-5P
433962-93-7P 433962-95-9P 433962-97-1P 433962-99-3P 433963-02-1P
433963-04-3P 433963-06-5P 433963-08-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of piperazinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT 93-55-0, 1-Phenylpropan-1-one 100-52-7, Benzaldehyde, reactions
106-57-0, Piperazine-2,5-dione 110-85-0, Piperazine, reactions
123-75-1, Pyrrolidine, reactions 142-73-4, ((Carboxymethyl)amino)acetic acid 443-69-6, 5-Fluoroisatin 446-22-0, 1-(2-Fluorophenyl)propan-1-one
456-03-1, 1-(4-Fluorophenyl)propan-1-one 585-32-0, 2-Phenyl-2-propylamine 600-18-0, 2-Oxobutyric acid 711-33-1, 1-(4-Trifluoromethylphenyl)propan-1-one 1562-34-1, Phenyl vinylsulfonate
1663-39-4, tert-Butyl acrylate 1932-03-2, 1-(2-Chloroethyl)piperidine
2627-86-3, (S)-1-Phenylethylamine 3680-02-2, Methyl vinyl sulfone
3789-59-1, (S)-1-Phenylpropylamine 5006-62-2, Ethyl nipecotate
5625-67-2, Piperazine-2-one 5913-13-3 13623-94-4, 1,1-Bis(methylsulfanyl)-2-nitroethene 13688-56-7, Trimethylsilyl methacrylate 14268-66-7, 3,4-Methylenedioxyaniline 17430-98-7, (S)-1-Cyclohexylethylamine 17630-76-1, 5-Chloroisatin 19072-67-4
22013-33-8, 2,3-Dihydrobenzo[1,4]dioxin-6-ylamine 22286-82-4, 2-Phenylacrylic acid ethyl ester 41851-59-6, (S)-1-(4-Methoxyphenyl)ethylamine 59697-91-5, 2-Phenylbut-3-enoic acid ethyl ester 68906-26-3, (S)-2-Methyl-1-phenylpropylamine 76003-29-7, 3-Oxopiperazine-1-carboxylic acid tert-butyl ester 82796-69-8, (S)-1-(3-Methoxyphenyl)ethylamine 90917-86-5, 1-Phenylpiperazin-2-one
219312-89-7 425622-16-8, 3-Bromomethyl-2-phenylquinoline-4-carboxylic

acid ((S)-1-cyclohexylethyl)amide 433963-10-1 433963-14-5
433963-17-8 433963-21-4 433963-23-6 433963-26-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and
NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 5 OF 11 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 137:20302 MARPAT Full-text
TITLE: Preparation of 3-(piperidinylalkyl)-4-quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders
INVENTOR(S): Farina, Carlo; Giardina, Giuseppe; Grugni, Mario; Nadler, Guy Marguerite Marie Gerard
PATENT ASSIGNEE(S): Glaxosmithkline S.P.A., Italy; Laboratoire Glaxosmithkline S.A.S.
SOURCE: PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002044154	A1	20020606	WO 2001-EP13832	20011126
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002016060	A5	20020611	AU 2002-16060	20011126
EP 1339691	A1	20030903	EP 2001-998541	20011126
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004517079	T2	20040610	JP 2002-546524	20011126
US 2004102633	A1	20040527	US 2003-433595	20030925
PRIORITY APPLN. INFO.:			GB 2000-28964	20001128
			WO 2001-EP13832	20011126

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [wherein R1 = H or alkyl; R2 = R8R9; R3 = H or (un)substituted alkyl or cycloalkyl(alkyl); R4 = NR10R11; R5 = (un)substituted alkyl, cycloalkyl(alkyl), aryl, or single or fused-ring aromatic heterocyclic group; R6 = H, or 1-3 of alkyl, alkenyl, aryl, alkoxy, OH, halo, NO2, cyano, CO2H, carboxamido, sulfonamido,

alkoxycarbonyl, haloalkyl, acyloxy, (di)(alkyl)amino, alkoxyamido, alkoxycarboxylate, or an esterified derivative thereof; R7 = H or halo; n = 1-6; R8 = single bond or (un)substituted alkyl; R9 = (un)substituted cycloalkyl or (hetero)aryl; R10 and R11 = independently H or alkyl; or NR10R11 = (un)substituted, (un)saturated heterocycle; any of R1, R3, R5, R8, R9, R10, R11, or R12 may be (un)substituted 1 or more times by halo, OH, NH2, cyano, NO2, CO2H, or oxo; with 20 compds. excluded; and their pharmaceutically acceptable salts or hydrates] were prepared I are a novel class of potent non-peptide neurokinin-3 (NK-3) antagonists, some of which fall within the generic scope of WO 00/31037. I are far more stable metabolically and show improved oral bioavailability compared to the known peptidic NK-3 receptor antagonists (no data). In addition, I have good NK-2 antagonist activity and are considered to be of potential use in the prevention and treatment of a wide variety of clin. conditions which are characterized by over-stimulation of tachykinin receptors, in particular NK-3 and NK-2. Thirty-three specific compds. I were prepared For instance, 3-bromomethyl-2-phenylquinoline-4-carboxylic acid Me ester (preparation given) was subjected to the sequence of (1) amination of the bromide with 4-piperidinopiperidine (56%), (2) acid hydroylsis of the ester, (3) amidation with 3-hydroxybenzylamine (20.6%) to give the title compound II. In binding assays using human NK-2 and NK-3 receptors, the most potent I exhibited IC50 values ranging from 0.5 nM to 1000 nM and 0.1 nM to 1000 nM, resp.

IC ICM C07D215-52
ICS C07D401-06; C07D401-14; A61K031-47; A61P011-00

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

ST piperidinylalkyl quinolinecarboxamide prepn neurokinin receptor antagonist; NK2 NK3 receptor antagonist quinolinecarboxamide CNS agent; NK3 NK2 receptor antagonist quinolinecarboxamide respiratory disease treatment

IT AIDS (disease)
(AIDS dementia complex; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Mental disorder
(AIDS dementia; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Intestine, disease
(Crohn's; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Nervous system, disease
(Huntington's chorea; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

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(NK2 antagonists; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

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(Raynaud's phenomenon; preparation of piperidinylalkyl quinolinecarboxamides
as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
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(amyotrophic lateral sclerosis; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
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(angina pectoris; preparation of piperidinylalkyl quinolinecarboxamides as
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(depression; preparation of piperidinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
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(diabetic neuropathy; preparation of piperidinylalkyl quinolinecarboxamides
as NK-3 and NK-2 antagonists for treatment of respiratory diseases and

CNS disorders)
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Blood coagulation
(disorder; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and
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(eosinophilic; preparation of piperidinylalkyl quinolinecarboxamides as NK-3
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(gastroesophageal reflux; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
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(gastrointestinal; preparation of piperidinylalkyl quinolinecarboxamides as
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(hyperresponsiveness; preparation of piperidinylalkyl quinolinecarboxamides
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(inflammation; preparation of piperidinylalkyl quinolinecarboxamides as NK-3
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(inflammatory; preparation of piperidinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
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(migraine; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and
NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
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Pain

(neuralgia, chemotherapy-induced; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

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(neurogenic; preparation of piperidinylalkyl quinolinecarboxamides as NK-3
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IT Nerve, disease
(peripheral neuropathy; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Alcoholism
Allergy
Allergy inhibitors
Alzheimer's disease
Analgesics
Anti-Alzheimer's agents
Anti-inflammatory agents
Antianginal agents
Antiarthritics
Antiasthmatics
Anticonvulsants
Antidepressants
Antihypertensives
Antimigraine agents
Antiparkinsonian agents
Antipsychotics
Antirheumatic agents
Anxiety
Anxiolytics
Asthma
Bladder, disease
Cardiovascular agents
Connective tissue, disease
Cough
Down's syndrome
Drug dependence
Drugs
Eczema
Epilepsy
Human
Immunomodulators
Lupus erythematosus
Movement disorders
Multiple sclerosis
Nervous system agents
Osteoarthritis
Parkinson's disease

Preeclampsia
Pruritus
Psoriasis
Rheumatoid arthritis
Schizophrenia
Skin, disease
Stress, animal
Urticaria
(preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(proteinuria; preparation of piperidinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Mental disorder
(psychosis; preparation of piperidinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

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(reflex sympathetic dystrophy; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Nose, disease
(rhinitis; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and
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IT Connective tissue, disease
(scleroderma; preparation of piperidinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Mental disorder
(senile psychosis; preparation of piperidinylalkyl quinolinecarboxamides as
NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Multiple sclerosis
(therapeutic agents; preparation of piperidinylalkyl quinolinecarboxamides
as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Tachykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type NK2; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and
NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Tachykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type NK3; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and
NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Intestine, disease

(ulcerative colitis; preparation of piperidinylalkyl quinolinecarboxamides
as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Skin, disease
(wheal-flare reaction; preparation of piperidinylalkyl quinolinecarboxamides
as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT 433980-88-2P 433980-91-7P 433980-92-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(NK-2 and NK-3 receptor antagonist; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT 345235-05-4P 433980-78-0P 433980-79-1P 433980-80-4P 433980-81-5P
433980-82-6P 433980-83-7P 433980-84-8P 433980-85-9P 433980-86-0P
433980-87-1P 433980-89-3P 433980-90-6P 433980-93-9P 433980-94-0P
433980-95-1P 433980-96-2P 433980-97-3P 433980-98-4P 433980-99-5P
433981-00-1P 433981-01-2P 433981-02-3P 433981-03-4P 433981-04-5P
433981-05-6P 433981-06-7P 433981-07-8P 433981-08-9P 434307-25-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(NK-2 and NK-3 receptor antagonist; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT 74960-43-3P, 3-Methyl-2-phenylquinoline-4-carboxylic acid methyl ester
174636-71-6P, 3-Methyl-2-phenylquinoline-4-carbonyl chloride
191796-86-8P, 3-Methyl-2-phenylquinoline-4-carboxylic acid tert-butyl ester 270574-25-9P, 7-Methoxy-3-methyl-2-phenylquinoline-4-carboxylic acid methyl ester 270574-26-0P, 3-[[[1,4']Bipiperidinyl-1'-yl]methyl]-8-bromo-7-methoxy-2-phenylquinoline-4-carboxylic acid methyl ester
270574-27-1P 272104-64-0P, 3-Bromomethyl-2-phenylquinoline-4-carboxylic acid methyl ester 345235-03-2P 345235-09-8P 433712-63-1P,
3-Bromomethyl-2-phenylquinoline-4-carboxylic acid tert-butyl ester
433963-14-5P 433981-09-0P, 3-[1,4'-Bipiperidinyl-1'-yl]-2-phenylquinoline-4-carboxylic acid methyl ester 433981-10-3P,
3-[[1,4']Bipiperidinyl-1'-yl]-2-phenylquinoline-4-carboxylic acid dihydrochloride 433981-11-4P, 4-[1-Benzylpiperidin-4-yl]piperazine-1-carboxylic acid 9H-fluoren-9-ylmethyl ester 433981-12-5P,
4-[Piperidin-4-yl]piperazine-1-carboxylic acid 9H-fluoren-9-ylmethyl ester
433981-13-6P, 3-[[4-[4-[9H-Fluoren-9-ylmethoxycarbonyl]piperazin-1-yl]piperidin-1-yl]methyl]-2-phenylquinoline-4-carboxylic acid methyl ester
433981-14-7P, 3-[[4-[4-[9H-Fluoren-9-ylmethoxycarbonyl]piperazin-1-yl]piperidin-1-yl]methyl]-2-phenylquinoline-4-carboxylic acid
433981-15-8P 433981-16-9P 433981-17-0P 433981-18-1P 433981-19-2P
433981-20-5P 433981-21-6P 433981-22-7P 433981-23-8P 433981-25-0P
433981-26-1P 433981-27-2P 433981-28-3P 433981-29-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of piperidinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT 93-55-0 110-89-4, Piperidine, reactions 343-69-1 3612-20-2
3789-59-1 4897-50-1, 1,4'-Bipiperidine 5006-62-2 6341-92-0

7568-93-6, 1-Phenylethanolamine 17430-98-7 43071-45-0 73604-31-6
79099-07-3 91596-61-1 159874-26-7, [1,4'-Bipiperidin]-2-one
215190-22-0, 1-Fmoc-piperazine hydrochloride 220594-77-4,
3-Hydroxy-2-methyl-3-phenylpropylamine 221352-86-9 321863-61-0
433962-93-7 433963-17-8 433963-21-4 433963-26-9 433981-30-7,
7-Methoxy-3-methyl-2-phenylquinoline-4-carboxylic acid 433981-31-8
433981-32-9 433981-33-0 433981-34-1 433981-35-2 434307-26-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and
NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 6 OF 11 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 137:6099 MARPAT Full-text
TITLE: Preparation of 3-(piperidinylalkyl)-4-quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders
INVENTOR(S): Farina, Carlo; Giardina, Giuseppe; Grugni, Mario; Nadler, Guy Marguerite Marie Gerard
PATENT ASSIGNEE(S): Glaxosmithkline S.P.A., Italy; Laboratoire Glaxosmithkline S.A.S.
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002043734	A1	20020606	WO 2001-EP14140	20011127
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002021923	A5	20020611	AU 2002-21923	20011127
EP 1337253	A1	20030827	EP 2001-998350	20011127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004519432	T2	20040702	JP 2002-545704	20011127
PRIORITY APPLN. INFO.:			GB 2000-28963	20001128
			GB 2001-9120	20010411
			WO 2001-EP14140	20011127

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [wherein R1 = H or alkyl; R2 = (hetero)aryl or cycloalkyl; R3 = H or alkyl, (un)substituted by 1 or more fluorines; R4 = NR8R9 or R12; R5 = branched or linear alkyl, cycloalkyl(alkyl), aryl, or single or fused-ring aromatic heterocyclic group; R6 = H, or 1-3 of alkyl, alkenyl, aryl, alkoxy, OH, halo, NO2, cyano, CO2H, carboxamido, sulfonamido, alkoxycarbonyl, CF3, acyloxy, or (di)(alkyl)amino; R7 = H or halo; n = 1-6; R8 = H or Me; R9 = H, (cyclo)alkyl, aryl, or R10R11; or R8R9 form an (un)substituted heterocyclic ring; R10 = (cyclo)alkyl or aryl; R11 = carboxy or alkylcarboxy; R12 = R13 or OR13; R13 = H or alkyl or aryl, (un)substituted by 1 or more fluorines; any of R2, R5, R9, and R10 may be (un)substituted 1 or more times by halo, OH, NH2, cyano, NO2, CO2H, or oxo; with 1 compound excluded; and their pharmaceutically acceptable salts or hydrates] were prepared I are a novel class of potent non-peptide neurokinin-3 (NK-3) antagonists, some of which fall within the generic scope of WO 00/31037. I are far more stable metabolically and show improved oral bioavailability compared to the known peptidic NK-3 receptor antagonists (no data). In addition, I have good NK-2 antagonist activity and are considered to be of potential use in the prevention and treatment of a wide variety of clin. conditions which are characterized by over-stimulation of tachykinin receptors, in particular NK-3 and NK-2. Eleven specific (S)-isomeric compds. I were prepared, and their general stereochem. forms are claimed. For instance, 3-methyl-2-phenylquinoline-4-carbonyl chloride (6-step preparation given) was subjected to a sequence of (1) t-Bu esterification (17.2%), (2) α-bromination (80%), (3) amination of the bromide with 4-[(1-piperidin-4-ylmethanoyl)amino]benzoic acid Et ester (80%), (4) ester hydrolysis, and (5) amidation with (S)-(+)-1-cyclohexylethylamine (90%) to give the title compound II. In binding assays using human NK-2 receptors, the most potent I had IC50 values ranging from 0.5 nM to 1000 nM.

IC ICM A61K031-47

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

ST piperidinylalkyl quinolinecarboxamide prepn neurokinin receptor antagonist; NK2 NK3 receptor antagonist quinolinecarboxamide CNS agent; NK3 NK2 receptor antagonist quinolinecarboxamide respiratory disease treatment

IT AIDS (disease)
(AIDS dementia complex; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Mental disorder
(AIDS dementia; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Intestine, disease
(Crohn's; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Nervous system, disease
(Huntington's chorea; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Tachykinin receptors
(NK2 antagonists; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS

disorders)
IT Tachykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NK3 antagonists; preparation of piperidinylalkyl quinolinecarboxamides as
NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Blood vessel, disease
(Raynaud's phenomenon; preparation of piperidinylalkyl quinolinecarboxamides
as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Eye, disease
(allergic conjunctivitis; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Nervous system, disease
(amyotrophic lateral sclerosis; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Heart, disease
(angina pectoris; preparation of piperidinylalkyl quinolinecarboxamides as
NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Dermatitis
(atopic; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and
NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Lung, disease
(chronic obstructive; preparation of piperidinylalkyl quinolinecarboxamides
as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Eye, disease
(conjunctivitis; preparation of piperidinylalkyl quinolinecarboxamides as
NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Dermatitis
(contact; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and
NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Nervous system, disease
(degeneration; preparation of piperidinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Nerve, disease
(demyelination; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Mental disorder
(depression; preparation of piperidinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS

disorders)
IT Nerve, disease
(diabetic neuropathy; preparation of piperidinylalkyl quinolinecarboxamides
as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Appetite
Blood coagulation
(disorder; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and
NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Blood pressure
(elevation; preparation of piperidinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Fasciola
(eosinophilic; preparation of piperidinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Digestive tract, disease
(gastroesophageal reflux; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Drugs
(gastrointestinal; preparation of piperidinylalkyl quinolinecarboxamides as
NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Respiratory tract, disease
(hyperresponsiveness; preparation of piperidinylalkyl quinolinecarboxamides
as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Bladder, disease
(incontinence; preparation of piperidinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Eye, disease
(inflammation; preparation of piperidinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Intestine, disease
Pain
(inflammatory; preparation of piperidinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Intestine, disease
(irritable bowel syndrome; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Headache
(migraine; preparation of piperidinylalkyl quinolinecarboxamides as NK-3

and
NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Nerve, disease
Pain
(neuralgia, chemotherapy-induced; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Inflammation
(neurogenic; preparation of piperidinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Nerve, disease
(neuropathy, AIDS-related or chemotherapy-induced; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Mental disorder
(neurotic depression; preparation of piperidinylalkyl quinolinecarboxamides
as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Nerve, disease
(peripheral neuropathy; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
IT Alcoholism
Allergy
Allergy inhibitors
Alzheimer's disease
Analgesics
Anti-Alzheimer's agents
Anti-inflammatory agents
Antianginal agents
Antiarthritics
Antiasthmatics
Anticonvulsants
Antidepressants
Antihypertensives
Antimigraine agents
Antiparkinsonian agents
Antipsychotics
Antirheumatic agents
Anxiety
Anxiolytics
Asthma
Bladder, disease
Cardiovascular agents
Connective tissue, disease
Cough
Down's syndrome
Drug dependence
Drugs
Eczema
Epilepsy
Fibrosis
Human
Immunomodulators

Lupus erythematosus
Movement disorders
Multiple sclerosis
Nervous system agents
Osteoarthritis
Parkinson's disease
Preeclampsia
Pruritus
Psoriasis
Rheumatoid arthritis
Schizophrenia
Skin, disease
Stress, animal
Urticaria
(preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(proteinuria; preparation of piperidinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Mental disorder
(psychosis; preparation of piperidinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Nervous system, disease
(reflex sympathetic dystrophy; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Nose, disease
(rhinitis; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and
NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Connective tissue, disease
(scleroderma; preparation of piperidinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Mental disorder
(senile psychosis; preparation of piperidinylalkyl quinolinecarboxamides as
NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Multiple sclerosis
(therapeutic agents; preparation of piperidinylalkyl quinolinecarboxamides
as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Tachykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type NK2; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and
NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Tachykinin receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type NK3; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and
NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Intestine, disease
(ulcerative colitis; preparation of piperidinylalkyl quinolinecarboxamides
as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT Skin, disease
(wheal-flare reaction; preparation of piperidinylalkyl quinolinecarboxamides
as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT 433712-68-6P, 4-[[1-[1-[4-((S)-1-Cyclohexylethylcarbamoyl)-2-phenylquinolin-3-ylmethyl]piperidin-4-yl]methanoyl]amino]benzoic acid ethyl ester 433712-69-7P, 3-[[1-[1-[4-((S)-1-Cyclohexylethylcarbamoyl)-2-phenylquinolin-3-ylmethyl]piperidin-4-yl]methanoyl]amino]benzoic acid ethyl ester 433712-77-7P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(NK-3 and NK-2 antagonist; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT 433712-70-0P, 4-[[1-[1-[4-((S)-1-Cyclohexylethylcarbamoyl)-2-phenylquinolin-3-ylmethyl]piperidin-4-yl]methanoyl]amino]benzoic acid 433712-71-1P, 3-[[1-[1-[4-((S)-1-Cyclohexylethylcarbamoyl)-2-phenylquinolin-3-ylmethyl]piperidin-4-yl]methanoyl]amino]benzoic acid 433712-72-2P 433712-73-3P 433712-74-4P 433712-75-5P 433712-76-6P 433712-78-8P, 1-[4-((S)-1-Cyclohexylethylcarbamoyl)-2-phenylquinolin-3-ylmethyl]piperidine-4-carboxylic acid hydrochloride 433712-79-9P 433712-80-2P 433712-81-3P 433712-82-4P 433712-83-5P 433712-84-6P 433712-85-7P 433712-86-8P 433712-87-9P 433712-88-0P 433712-89-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(NK-3 and NK-2 antagonist; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT 174636-71-6P, 3-Methyl-2-phenylquinoline-4-carbonyl chloride 191796-86-8P, 3-Methyl-2-phenylquinoline-4-carboxylic acid tert-butyl ester 425622-15-7P, 3-Methyl-2-phenylquinoline-4-carboxylic acid ((S)-1-cyclohexylethyl)amide 425622-16-8P, 3-Bromomethyl-2-phenylquinoline-4-carboxylic acid ((S)-1-cyclohexylethyl)amide 433712-58-4P, 4-Chlorocarbonylpiperidine-1-carboxylic acid 9H-fluoren-9-ylmethyl ester 433712-59-5P, 4-(4-Ethoxycarbonylphenylcarbamoyl)piperidine-1-carboxylic acid 9H-fluoren-9-ylmethyl ester 433712-60-8P, 4-(3-Ethoxycarbonylphenylcarbamoyl)piperidine-1-carboxylic acid 9H-fluoren-9-ylmethyl ester 433712-61-9P, 4-[(1-Piperidin-4-ylmethanoyl)amino]benzoic acid ethyl ester 433712-62-0P, 3-[(1-Piperidin-4-ylmethanoyl)amino]benzoic acid ethyl ester 433712-63-1P, 3-Bromomethyl-2-phenylquinoline-4-carboxylic acid tert-butyl ester 433712-64-2P, 3-[4-(4-Ethoxycarbonylphenylcarbamoyl)piperidin-1-ylmethyl]-2-phenylquinoline-4-carboxylic acid tert-butyl ester 433712-65-3P, 3-[4-(3-Ethoxycarbonylphenylcarbamoyl)piperidin-1-ylmethyl]-

2-phenylquinoline-4-carboxylic acid tert-butyl ester 433712-66-4P, 3-[4-(4-Ethoxycarbonylphenylcarbamoyl)piperidin-1-ylmethyl]-2-phenylquinoline-4-carboxylic acid 433712-67-5P, 3-[4-(3-Ethoxycarbonylphenylcarbamoyl)piperidin-1-ylmethyl]-2-phenylquinoline-4-carboxylic acid
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of piperidinylalkyl quinolinecarboxamides as NK-3
and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

IT 94-09-7, Ethyl 4-aminobenzoate 110-89-4, Piperidine, reactions 582-33-2, Ethyl 3-aminobenzoate 1126-09-6, 4-Ethoxycarbonylpiperidine 17430-98-7, (S)-1-Cyclohexylethylamine 35090-95-0, 1-(4-Piperidinylcarbonyl)pyrrolidine 43071-45-0, 3-Methyl-2-phenylquinoline-4-carboxylic acid 148928-15-8, Fmoc-isonipecotic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of piperidinylalkyl quinolinecarboxamides as NK-3 and
NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 7 OF 11 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 136:386030 MARPAT Full-text
TITLE: Quinoline derivatives as NK-3 and NK-2 antagonists
INVENTOR(S): Farina, Carlo; Gagliardi, Stefania; Giardina, Giuseppe; Grugni, Mario; Martinelli, Marisa; Nadler, Guy Marguerite Marie Gerard
PATENT ASSIGNEE(S): Glaxosmithkline S.p.A., Italy; Laboratoire Glaxosmithkline
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002038547	A1	20020516	WO 2001-EP13139	20011112
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002020702	A5	20020521	AU 2002-20702	20011112
EP 1334089	A1	20030813	EP 2001-993602	20011112
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004517062	T2	20040610	JP 2002-541083	20011112
US 2004082589	A1	20040429	US 2003-416596	20031023
PRIORITY APPLN. INFO.:			GB 2000-27696	20001113

GB 2001-9119 20010411
WO 2001-EP13139 20011112

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I and their pharmaceutically acceptable salts or hydrates are claimed [wherein: R1 = H or alkyl; R2 = aryl, cycloalkyl, or heteroaryl; R3 = H or C1-3 alkyl, (un)substituted by 1 or more fluorines; R4 = H, R8NR9R10, R11R13, or R11R12R13; R5 = branched or linear alkyl, cycloalkyl(alkyl), aryl(alkyl), or single or fused-ring aromatic heterocyclic group; R6 = H, or 1-3 of alkyl, alkenyl, aryl, alkoxy, OH, halo, NO2, cyano, CO2H, carboxamido, sulfonamido, alkoxycarbonyl, CF3, acyloxy, (di)(alkyl)amino; R7 = H, halo; n = 1-6; R8 = bond or alkylene; R9, R10 = H, alkyl, cycloalkyl(alkyl), aryl(alkyl); or NR9R10 = (un)saturated (fluoro)heterocyclyl; R11 = alkyl, alkenyl, (hetero)aryl, (un)saturated carbocyclyl with ≥1 N/O/S atom(s), cycloalkyl, etc.; R12 = (un)substituted alkyl, alkoxy; R13 = H, CO2R14; R14 = H, alkyl; any of R2, R5, R8, R9, R10, R11, R12, and R14 may be substituted by halo, OH, amino, cyano, NO2, CO2H, or oxo; with specific exclusion of 14 compds.]. Also claimed is a process for preparing the compds., pharmaceutical compns. comprising them, and their use in medicine. I are a novel class of potent non-peptide NK-3 antagonists, some of which fall within the generic scope of WO 00/31037. I are also far more stable from a metabolic point of view than the known peptidic NK-3 receptor antagonists (no data), and are of potential therapeutic utility. I also have good NK-2 antagonist activity, and are therefore considered to be of potential use in the prevention and treatment of a wide variety of clin. conditions which are characterized by overstimulation of tachykinin receptors, in particular NK-3 and NK-2. I also show improved oral bioavailability (no data). Approx. 25 specific (S)-isomeric compds. I were prepared, and their general stereochem. forms are claimed. For instance, 3-methyl-2-phenylquinoline-4-carboxylic acid was subjected to a sequence of: (1) Me esterification; (2) α-bromination; (3) amination of the bromide with Fmoc-piperazine; (4) ester hydrolysis; (5) amidation with (S)-1-phenylpropylamine; (6) deprotection at Fmoc; (7) coupling with N-BOC-β-alanine; and (8) deprotection at BOC; to give title compound II, isolated as the di-HCl salt. In binding assays using human and guinea pig NK-3 receptors, and human NK-2 receptors, the most potent I had IC50 values in the range of 0.1-1000 nM for NK-3, and 0.5-1000 nM for NK-2. Antagonist behavior of I at NK-3 receptors was evidenced by reversal of the effects of senktide and NKB, and antagonist activity at NK-2 receptors was indicated by reversal of the effects of NKA.

IC ICM C07D215-52
ICS C07D401-12; A61K031-4709; A61P011-00

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

ST quinoline prepn neurokinin receptor antagonist; NK2 NK3 receptor antagonist quinoline antiinflammatory immunomodulator CNS cardiovascular

IT Tachykinin receptors
(NK2 antagonists; preparation of quinoline derivs. as NK-3 and NK-2 antagonists)

IT Tachykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NK3 antagonists; preparation of quinoline derivs. as NK-3 and NK-2 antagonists)

IT Drugs
(gastrointestinal; preparation of quinoline derivs. as NK-3 and NK-2 antagonists)
IT Anti-inflammatory agents
Cardiovascular agents
Human
Immunomodulators
Nervous system agents
(preparation of quinoline derivs. as NK-3 and NK-2 antagonists)
IT Tachykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type NK2; preparation of quinoline derivs. as NK-3 and NK-2 antagonists)
IT Tachykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type NK3; preparation of quinoline derivs. as NK-3 and NK-2 antagonists)
IT 425621-77-8P, 3-[4-[[4-[((S)-1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]-3-oxo-2-phenylpropionic acid ethyl ester
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of quinoline derivs. as NK-3 and NK-2 antagonists)
IT 425621-62-1P, (-)-(S)-N-(1-Phenylpropyl)-3-[[4-(3-aminopropionyl)piperazin-1-yl]methyl]-2-phenylquinoline-4-carboxamide dihydrochloride
425621-63-2P, 3-[1-[4-[[2-Phenyl-4-[((S)-1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]methanoyl]pyrazine-2-carboxylic acid
425621-64-3P, 4-[1-[4-[[2-Phenyl-4-[((S)-1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]methanoyl]nicotinic acid 425621-65-4P, [2-Oxo-2-[4-[[2-phenyl-4-[((S)-1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]ethoxy]acetic acid 425621-66-5P, [1-[2-Oxo-2-[4-[[2-phenyl-4-[((S)-1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]ethyl]cyclopentyl]acetic acid 425621-67-6P, 3,3-Dimethyl-5-oxo-5-[4-[[2-phenyl-4-[((S)-1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]pentanoic acid 425621-68-7P 425621-69-8P
425621-70-1P, (E)-4-Oxo-4-[4-[[2-phenyl-4-[((S)-1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]but-2-enoic acid
425621-71-2P, 3-[4-[[4-[((S)-1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]-3-oxopropionic acid 425621-72-3P, 5-[4-[[4-[((S)-1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]-5-oxopentanoic acid 425621-73-4P, 3-[1-[4-[[4-[((S)-1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]methanoyl]pyrazine-2-carboxylic acid
425621-74-5P, 3-[1-[4-[[4-[((S)-1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]methanoyl]benzoic acid
425621-75-6P, 5-[1-[4-[[4-[((S)-1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]methanoyl]nicotinic acid
425621-76-7P, 4-[1-[4-[[4-[((S)-1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]methanoyl]benzoic acid
425621-78-9P, 3-[4-[[4-[((S)-1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]-3-oxo-2-phenylpropionic acid sodium salt
425621-79-0P, 3-[(4-Formylpiperazin-1-yl)methyl]-2-phenylquinoline-4-carboxylic acid (S)-1-cyclohexylethylamide 425621-80-3P, (S)-N-(1-Cyclohexylethyl)-2-phenyl-3-[[4-(phenylcarbamoyl)piperazin-1-yl]methyl]quinoline-4-carboxamide 425621-81-4P, (S)-N-(1-Cyclohexylethyl)-2-phenyl-3-[(4-carbamoylpiperazin-1-yl)methyl]quinoline-4-carboxamide 425621-82-5P, 3-[[4-(3-Aminopropanoyl)piperazin-1-yl]methyl]-

2-phenylquinoline-4-carboxylic acid (S)-1-cyclohexylethylamide 425621-83-6P, 3-[[4-[3-(Ethylamino)propanoyl]piperazin-1-yl]methyl]-2-phenylquinoline-4-carboxylic acid (S)-1-cyclohexylethylamide 425621-84-7P, 2-Phenyl-3-[[4-[3-(pyrrolidin-1-yl)propanoyl]piperazin-1-yl]methyl]quinoline-4-carboxylic acid (S)-1-cyclohexylethylamide 425621-85-8P, 2-Phenyl-3-[[4-[3-(piperidin-1-yl)propanoyl]piperazin-1-yl]methyl]quinoline-4-carboxylic acid (S)-1-cyclohexylethylamide 425621-86-9P, N-(1-Phenylpropyl)-3-[[4-(3-aminopropionyl)piperazin-1-yl]methyl]-2-phenylquinoline-4-carboxamide 425621-87-0P, 3-[1-[4-[[2-Phenyl-4-[(1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]methanoyl]pyrazine-2-carboxylic acid 425621-88-1P, 4-[1-[4-[[2-Phenyl-4-[(1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]methanoyl]nicotinic acid 425621-89-2P, [2-Oxo-2-[4-[[2-phenyl-4-[(1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]ethoxy]acetic acid 425621-90-5P, [1-[2-Oxo-2-[4-[[2-phenyl-4-[(1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]ethyl]cyclopentyl]acetic acid 425621-91-6P, 3,3-Dimethyl-5-oxo-5-[4-[[2-phenyl-4-[(1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]pentanoic acid 425621-92-7P, 2-[1-[4-[[2-Phenyl-4-[(1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]methanoyl]cyclopropanecarboxylic acid 425621-93-8P, 2-[1-[4-[[2-Phenyl-4-[(1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]methanoyl]cyclohexanecarboxylic acid 425621-94-9P, 4-Oxo-4-[4-[[2-phenyl-4-[(1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]but-2-enoic acid 425621-95-0P, 3-[4-[[4-[(1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]-3-oxopropionic acid 425621-96-1P, 5-[4-[[4-[(1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]-5-oxopentanoic acid 425621-97-2P, 3-[1-[4-[[4-[(1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]methanoyl]pyrazine-2-carboxylic acid 425621-98-3P, 3-[1-[4-[[4-[(1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]methanoyl]benzoic acid 425621-99-4P, 5-[1-[4-[[4-[(1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]methanoyl]nicotinic acid 425622-00-0P, 4-[1-[4-[[4-[(1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]methanoyl]benzoic acid 425622-01-1P, 3-[4-[[4-[(1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]-3-oxo-2-phenylpropionic acid ethyl ester 425622-02-2P, 3-[4-[[4-[(1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]-3-oxo-2-phenylpropionic acid 425622-03-3P, 3-[(4-Formylpiperazin-1-yl)methyl]-2-phenylquinoline-4-carboxylic acid (1-cyclohexylethyl)amide 425622-04-4P, N-(1-Cyclohexylethyl)-2-phenyl-3-[[4-(phenylcarbamoyl)piperazin-1-yl]methyl]quinoline-4-carboxamide 425622-05-5P, N-(1-Cyclohexylethyl)-2-phenyl-3-[(4-carbamoylpiperazin-1-yl)methyl]quinoline-4-carboxamide 425622-06-6P, 3-[[4-(3-Aminopropanoyl)piperazin-1-yl]methyl]-2-phenylquinoline-4-carboxylic acid (1-cyclohexylethyl)amide 425622-07-7P, 3-[[4-[3-(Ethylamino)propanoyl]piperazin-1-yl]methyl]-2-phenylquinoline-4-carboxylic acid (1-cyclohexylethyl)amide 425622-08-8P, 2-Phenyl-3-[[4-[3-(pyrrolidin-1-yl)propanoyl]piperazin-1-yl]methyl]quinoline-4-carboxylic acid 1-cyclohexylethylamide 425622-09-9P, 2-Phenyl-3-[[4-[3-(piperidin-1-yl)propanoyl]piperazin-1-yl]methyl]quinoline-4-carboxylic acid (1-cyclohexylethyl)amide 425622-10-2P, 3-[1-[4-[[2-Phenyl-4-[(S)-1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]methanoyl]isonicotinic acid
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(drug candidate; preparation of quinoline derivs. as NK-3 and NK-2 antagonists)

IT 57260-71-6P, N-BOC-piperazine 74960-43-3P, 3-Methyl-2-phenylquinoline-4-carboxylic acid methyl ester 216372-65-5P, 2-Phenyl-3-(piperazin-1-ylmethyl)quinoline-4-carboxylic acid (S)-1-phenylpropylamide 270573-35-8P, 2-Phenyl-3-(piperazin-1-ylmethyl)quinoline-4-carboxylic acid (S)-1-cyclohexylethylamide 270574-10-2P, 3-[(4-Fmoc-piperazin-1-yl)methyl]-2-phenylquinoline-4-carboxylic acid methyl ester 270574-12-4P, 3-[(4-Fmoc-piperazin-1-yl)methyl]-2-phenylquinoline-4-carboxylic acid (S)-1-phenylpropylamide 270574-13-5P, 3-[(4-Fmoc-piperazin-1-yl)methyl]-2-phenylquinoline-4-carboxylic acid (S)-1-cyclohexylethylamide 272104-64-0P, 3-(Bromomethyl)-2-phenylquinoline-4-carboxylic acid methyl ester 425622-11-3P, 3-[(4-Fmoc-piperazin-1-yl)methyl]-2-phenylquinoline-4-carboxylic acid hydrochloride 425622-12-4P, 3-[(4-Fmoc-piperazin-1-yl)methyl]-2-phenylquinoline-4-carboxylic acid (S)-1-phenylethylamide 425622-13-5P, 2-Phenyl-3-(piperazin-1-ylmethyl)quinoline-4-carboxylic acid (S)-1-phenylethylamide 425622-14-6P, [3-Oxo-3-[4-[[2-phenyl-4-[((S)-1-phenylpropyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]propyl]carbamic acid tert-butyl ester 425622-15-7P, 3-Methyl-2-phenylquinoline-4-carboxylic acid (S)-1-cyclohexylethylamide 425622-16-8P, 3-(Bromomethyl)-2-phenylquinoline-4-carboxylic acid (S)-1-cyclohexylethylamide 425622-17-9P, 4-[[4-[((S)-1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazine-1-carboxylic acid tert-butyl ester 425622-18-0P, 3-[(4-Acryloylpiperazin-1-yl)methyl]-2-phenylquinoline-4-carboxylic acid (S)-1-cyclohexylethylamide
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of quinoline derivs. as NK-3 and NK-2 antagonists)

IT 103-71-9, Phenyl isocyanate, reactions 110-85-0, Piperazine, reactions 123-75-1, Pyrrolidine, reactions 814-68-6, Acryloyl chloride 3303-84-2 3789-59-1, (S)-1-Phenylpropylamine 4744-50-7, 2,3-Pyrazinedicarboxylic anhydride 17430-98-7, (S)-1-Cyclohexylethylamine 26371-07-3, 3-Piperidin-1-ylpropionic acid 43071-45-0, 3-Methyl-2-phenylquinoline-4-carboxylic acid 54635-33-5, 2-(Chlorocarbonyl)-2-phenylacetic acid ethyl ester 219312-89-7, 1-Fmoc-piperazine
RL: RCT (Reactant); RACT (Reactant or reagent)
(precursor; preparation of quinoline derivs. as NK-3 and NK-2 antagonists)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 8 OF 11 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 136:369740 MARPAT Full-text
TITLE: Preparation of piperazinylalkylquinoline-4-carboxamides as NK-3 and NK-2 receptor antagonists
INVENTOR(S): Farina, Carlo; Giardina, Giuseppe; Grugni, Mario; Nadler, Guy Marguerite Marie Gerard
PATENT ASSIGNEE(S): Glaxosmithkline S.p.A., Italy; Laboratoire Glaxosmithkline S.A.S.
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002038548	A1	20020516	WO 2001-EP13141	20011112
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002015043	A5	20020521	AU 2002-15043	20011112
EP 1334088	A1	20030813	EP 2001-983584	20011112
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004513165	T2	20040430	JP 2002-541084	20011112
US 2004077658	A1	20040422	US 2003-416600	20031023
PRIORITY APPLN. INFO.:			GB 2000-27701	20001113
			WO 2001-EP13141	20011112

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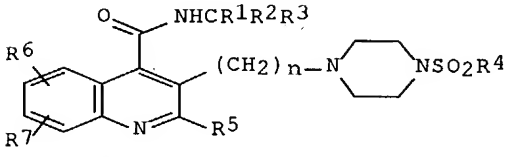


I

AB Title compds. [I; R1 = H , alkyl; R2 = aryl, cycloalkyl, heteroaryl; R3 = H, alkyl, optionally substituted by ≥1 F; R4 = R8R9; R8 = bond, alkyl, aryl; R9 = H, COO R10, NR11R12; R10 = H, alkyl; R11, R12 = H, alkyl; R5 = alkyl, cycloalkyl, cycloalkylalkyl, aryl, single or fused ring heteroaryl; R6 = H, alkyl, alkenyl, aryl, alkoxy, OH, halo, NO2, cyano, carboxy, carboxamido, sulfonamido, alkoxycarbonyl, CF3, acyloxy, amino; R7 = H, halo; n = 1-6; any of R2, R5, R8, R10, R11, R12 may be substituted by halo, hydroxy, amino, cyano, NO2, CO2H, oxo], were prepared Thus, 2-phenyl-3-piperazin-1-ylmethylquinoline-4-carboxylic acid ((S)-2-methyl-1-phenylpropyl)amide (preparation given) in MeCN was treated with EtO2CCH2CH2SO2Cl and diisopropylethylamine; the mixture was stirred 15 h at room temperature and for 3 h at 50° to give 3-[4-[4-((S)-2-methyl-1-phenylpropylcarbamoyl)-2-phenylquinolin-3-ylmethyl]piperazine-1-sulfonyl]propionic acid Me ester. The most potent I bind to NK-2 receptors with IC50 = 0.5-1000 nM.

IC ICM C07D215-52
ICS A61K031-47; A61K031-4709; A61P011-06

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

ST piperazinylalkylquinolinecarboxamide prepn NK3 NK2 antagonist; neurokinin antagonist piperazinylmethylquinolinecarboxamide prepn; quinolinecarboxamide piperazinylalkyl prepn neurokinin antagonist

IT Tachykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(type NK2, antagonists; preparation of piperazinylalkylquinoline-4-carboxamides as NK-3 and NK-2 receptor antagonists)

IT Tachykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type NK3, antagonists; preparation of piperazinylalkylquinoline-4-carboxamides as NK-3 and NK-2 receptor antagonists)

IT 216372-65-5P 270574-14-6P 270574-15-7P 423767-67-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of)

IT 423767-62-8P 423767-63-9P 423767-64-0P 423767-65-1P 423767-66-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazinylalkylquinoline-4-carboxamides as NK-3 and NK-2 receptor antagonists)

IT 98-09-9, Benzenesulfonyl chloride 109-89-7, Diethylamine, reactions 124-63-0, Methanesulfonyl chloride 1622-32-8, 2-Chloroethylsulfonyl chloride 3789-59-1, (S)-1-Phenylpropylamine 15441-07-3 17430-98-7, (S)-1-Cyclohexylethylamine 43071-45-0 68906-26-3 219312-89-7 270573-35-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of piperazinylalkylquinoline-4-carboxamides as NK-3 and NK-2 receptor antagonists)

IT 74960-43-3P, 4-Quinolinecarboxylic acid, 3-methyl-2-phenyl-, methyl ester 270574-10-2P 270574-11-3P 270574-12-4P 270574-13-5P 272104-64-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperazinylalkylquinoline-4-carboxamides as NK-3 and NK-2 receptor antagonists)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 9 OF 11 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 133:4605 MARPAT Full-text
TITLE: Preparation of quinoline-4-carboxamide derivatives as NK-3 and NK-2 receptor antagonists
INVENTOR(S): Farina, Carlo; Giardina, Giuseppe; Grugni, Mario; Morvan, Marcel; Nadler, Guy Margueritte Marie Gerard; Raveglia, Luca Francesco
PATENT ASSIGNEE(S): Smithkline Beecham S.P.A., Italy; Smithkline Beecham Laboratoires Pharmaceutiques
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000031037	A1	20000602	WO 1999-EP9115	19991119

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,

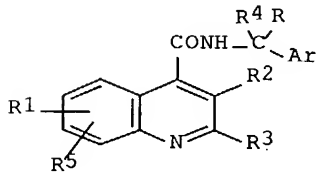
MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1131295	A1	20010912	EP 1999-961001	19991119
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200101412	T2	20011022	TR 2001-20010141219991119	
BR 9915475	A	20011218	BR 1999-15475	19991119
NZ 511777	A	20031219	NZ 1999-511777	19991119
AU 768708	B2	20040108	AU 2000-17770	19991119
NO 2001002473	A	20010718	NO 2001-2473	20010518
ZA 2001004071	A	20030107	ZA 2001-4071	20010518
US 2003212101	A1	20031113	US 2003-358938	20030205
US 6780875	B2	20040824		

PRIORITY APPLN. INFO.:

GB 1998-25552	19981120
GB 1998-25553	19981120
WO 1999-EP9115	19991119
US 2001-856085	20010904
US 2002-159218	20020531

GI



I

AB The title compds. of formula I [Ar = optionally substituted aryl or a C5-7 cycloalkdienyl group, or an optionally substituted C5-7 cycloalkyl group, or an optionally substituted single or fused ring aromatic heterocyclic group; R = H, linear or branched C1-6 alkyl, C3-7 cycloalkyl, C3-7 cycloalkylalkyl, R1 = H or up to three optional substituents selected from the list consisting of: C1-6 alkyl, C1-6 alkenyl, aryl, C1-6 alkoxy, OH, halogen, NO2, CN, etc; R2 = (CH2)nNY1Y2; n = an integer ranging from 1 - 9; Y1, Y2 independently = (un)substituted C1-6 alkyl or together with N to which they are attached represent optionally substituted N linked single or fused ring heterocyclic group; R3 = branched or linear C1-6 alkyl, C3-7 cycloalkyl, C4-7 cycloalkyl, etc; R4 = H, C1-6 alkyl; R5 = H, halogen] useful as NK-3 and NK-2 receptor antagonists (no data given) are prepared

IC ICM C07D215-52
ICS A61K031-47; C07D401-06; C07D471-10; C07D401-12; C07D401-14; C07D487-04; C07D491-10; C07D487-10; C07D413-10; C07D417-12; C07D471-10; C07D235-00; C07D221-00; C07D487-04; C07D241-00; C07D209-00; C07D491-10; C07D317-00; C07D221-00

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

ST quinolinecarboxamide prepn nk3 nk2 receptor antagonist

IT Intestine, disease
(Crohn's; preparation and effect of quinoline-4-carboxamide derivs.)
IT Nervous system
(Huntington's chorea; preparation and effect of quinoline-4-carboxamide derivs.)
IT Tachykinin receptors
(NK2 antagonists; quinoline-4-carboxamide derivs.)
IT Tachykinin receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NK3, antagonists; quinoline-4-carboxamide derivs.)
IT Heart, disease
(angina pectoris; preparation and effect of quinoline-4-carboxamide derivs.)
IT Eye, disease
(conjunctivitis; preparation and effect of quinoline-4-carboxamide derivs.)
IT Skin, disease
(cutaneous wheal; preparation and effect of quinoline-4-carboxamide derivs.)
IT Mental disorder
(dementia; preparation and effect of quinoline-4-carboxamide derivs.)
IT Mental disorder
(depression; preparation and effect of quinoline-4-carboxamide derivs.)
IT Connective tissue
Respiratory tract
(disease; preparation and effect of quinoline-4-carboxamide derivs.)
IT Appetite
(disorder; preparation and effect of quinoline-4-carboxamide derivs.)
IT Connective tissue
(fibrositis; preparation and effect of quinoline-4-carboxamide derivs.)
IT Digestive tract
(gastroesophageal reflux; preparation and effect of quinoline-4-carboxamide derivs.)
IT Fasciola
(infection with; preparation and effect of quinoline-4-carboxamide derivs.)
IT Intestine, disease
(irritable bowel syndrome; preparation and effect of quinoline-4-carboxamide derivs.)
IT Headache
(migraine; preparation and effect of quinoline-4-carboxamide derivs.)
IT Nerve, disease
(neuralgia; preparation and effect of quinoline-4-carboxamide derivs.)
IT AIDS (disease)
Alcoholism
Alzheimer's disease
Asthma
Cough
Down's syndrome
Eczema
Multiple sclerosis
Osteoarthritis
Parkinson's disease
Psoriasis
Schizophrenia

(preparation and effect of quinoline-4-carboxamide derivs.)
IT Mental disorder
(psychosis; preparation and effect of quinoline-4-carboxamide derivs.)
IT Analgesics
Anti-inflammatory agents
(quinoline-4-carboxamide derivs.)
IT Nose
(rhinitis; preparation and effect of quinoline-4-carboxamide derivs.)
IT Connective tissue
(scleroderma; preparation and effect of quinoline-4-carboxamide derivs.)
IT Lupus erythematosus
(systemic; preparation and effect of quinoline-4-carboxamide derivs.)
IT Intestine, disease
(ulcerative colitis; preparation and effect of quinoline-4-carboxamide derivs.)
IT 270573-00-7P 270573-01-8P 270573-02-9P 270573-03-0P 270573-04-1P
270573-05-2P 270573-06-3P 270573-07-4P 270573-08-5P 270573-09-6P
270573-10-9P 270573-11-0P 270573-12-1P 270573-13-2P 270573-14-3P
270573-15-4P 270573-16-5P 270573-17-6P 270573-18-7P 270573-19-8P
270573-20-1P 270573-21-2P 270573-22-3P 270573-23-4P 270573-24-5P
270573-25-6P 270573-26-7P 270573-27-8P 270573-28-9P 270573-29-0P
270573-31-4P 270573-32-5P 270573-34-7P 270573-35-8P 270573-36-9P
270573-37-0P 270573-38-1P 270573-39-2P 270573-40-5P 270573-41-6P
270573-42-7P 270573-43-8P 270573-44-9P 270573-45-0P 270573-46-1P
270573-47-2P 270573-48-3P 270573-49-4P 270573-50-7P 270573-51-8P
270573-52-9P 270573-53-0P 270573-55-2P 270573-56-3P 270573-57-4P
270573-58-5P 270573-59-6P 270573-60-9P 270573-61-0P 270573-62-1P
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270573-80-3P 270573-81-4P 270573-82-5P 270573-83-6P 270573-84-7P
270573-85-8P 270573-87-0P 270573-88-1P 270573-90-5P 270573-91-6P
270573-92-7P 270573-93-8P 270573-94-9P 270573-95-0P 270573-96-1P
270573-97-2P 270573-98-3P 270573-99-4P 270574-00-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinoline-4-carboxamide derivs. as NK-3 and NK-2 receptor
antagonists)
IT 74-88-4, Methyl iodide, reactions 108-30-5, Succinic anhydride, reactions 123-75-1, Pyrrolidine, reactions 128-08-5, n-Bromosuccinimide 631-61-8, Ammonium acetate 771-99-3, 4-Phenylpiperidine 3789-59-1, (S)-(1-Phenylpropyl)amine 4318-42-7, 1-Isopropylpiperazine 4897-50-1, 4-Piperidinopiperidine 6972-41-4, 3-Diethylaminopropionic acid 10191-60-3, Dimethyl N-cyanodithioiminocarbonate 13068-10-5 13360-57-1, Dimethylsulfamoylchloride 17430-98-7, (S)-1-Cyclohexylethylamine 41661-47-6, 4-Oxopiperidine 43071-45-0 68906-26-3 76535-74-5 219312-89-7 270574-31-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of quinoline-4-carboxamide derivs. as NK-3 and NK-2 receptor
antagonists)
IT 19146-54-4P 98961-97-8P 216372-53-1P 216372-65-5P 253176-45-3P
270574-01-1P 270574-02-2P 270574-03-3P 270574-04-4P 270574-05-5P
270574-07-7P 270574-08-8P 270574-09-9P 270574-10-2P 270574-11-3P
270574-12-4P 270574-13-5P 270574-14-6P 270574-15-7P 270574-16-8P

270574-17-9P 270574-18-0P 270574-19-1P 270574-20-4P 270574-21-5P
270574-22-6P 270574-23-7P 270574-24-8P 270574-25-9P 270574-26-0P
270574-27-1P 270574-28-2P 270574-29-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of quinoline-4-carboxamide derivs. as NK-3 and NK-2 receptor antagonists)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 10 OF 11 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 127:95204 MARPAT Full-text
TITLE: Preparation of quinoline-4-carboxamides and their use as neurokinin-3 and neurokinin-2 receptor antagonists
INVENTOR(S): Giardina, Giuseppe Arnaldo Maria; Grugni, Mario; Raveglia, Luca Francesco; Farina, Carlo
PATENT ASSIGNEE(S): Smithkline Beecham S.P.A., Italy; Giardina, Giuseppe Arnaldo Maria; Grugni, Mario; Raveglia, Luca Francesco; Farina, Carlo
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9719926	A1	19970605	WO 1996-EP5207	19961122
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
IT 1307330	B1	20011030	IT 1996-MI1688	19960802
CA 2238328	AA	19970605	CA 1996-2238328	19961122
AU 9710318	A1	19970619	AU 1997-10318	19961122
ZA 9609811	A	19980522	ZA 1996-9811	19961122
CN 1207729	A	19990210	CN 1996-199747	19961122
BR 9611757	A	19990406	BR 1996-11757	19961122
EP 1019377	A1	20000719	EP 1996-941025	19961122
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO				
JP 2000513325	T2	20001010	JP 1997-520158	19961122
TR 9800883	T2	20001221	TR 1998-9800883	19961122
TW 409123	B	20001021	TW 1996-85114501	19961123
NO 9802333	A	19980722	NO 1998-2333	19980522
US 2002068827	A1	20020606	US 2001-994402	20011126
PRIORITY APPLN. INFO.:			IT 1995-MI2462	19951124
			IT 1996-MI1688	19960802
			WO 1996-EP5207	19961122
			US 1998-77262	19980806
			US 2000-515336	20000605

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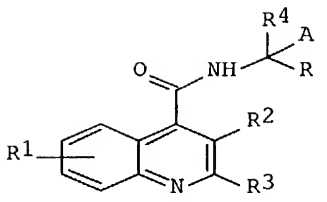

I

AB The title compds. [I; A = (un)substituted aryl, C5-7 cycloalkdienyl, (un)substituted single or fused ring aromatic heterocyclyl; R = (un)substituted C1-6 alkyl, C3-7 cycloalkyl, C3-7 cycloalkylalkyl, (un)substituted Ph, an optionally substituted five-membered heteroarom. ring, etc.; R1 = hydrogen or up to four substituents selected from C1-6 alkyl, C1-6 alkenyl, aryl, C1-6 alkoxy, hydroxy, halogen, nitro, cyano, carboxy, carboxamido, sulfonamido, C1-6 alkoxycarbonyl, trifluoromethyl, alkoxy, phthalimido, (un)substituted amino, etc.; R2 = hydrogen, C1-6 alkyl, hydroxy, halogen, cyano, (un)substituted amino, etc.; R3 = C1-6 alkyl, C3-7 cycloalkyl, C4-7 cycloalkylalkyl, (un)substituted aryl, (un)substituted single or fused ring aromatic heterocyclyl; R4 = hydrogen, C1-6 alkyl], useful as neurokinin 3 and neurokinin 2 receptor antagonists, are prepared Thus, (S)-N-(α-ethylbenzyl)-3-(2-aminoethoxy)-2-phenylquinoline-4-carboxamide was reacted with α,α'-dibromo-o- xylene and salified with HCl, producing (S)-N-(α-ethylbenzyl)-3-[2- (2-isoindolinyl)ethoxy]-2-phenylquinoline-4-carboxamide dihydrochloride (m.p. 95°; decomposition) which demonstrated a binding affinity in human neurokinin-3 receptors (expressed in CHO cell lines) against [125I]-[Me-Phe7]-neurokinin B of 1.2 nM.

IC ICM C07D215-52
ICS C07D401-12; C07D487-04; C07D401-06; A61K031-47

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

ST quinolinecarboxamide prepn neurokinin receptor antagonist; NK3 receptor antagonist prepn quinolinecarboxamide; NK2 receptor antagonist prepn quinolinecarboxamide

IT Intestine, disease
(Crohn's; quinoline-4-carboxamides for treatment of)

IT Tachykinin receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NK2 antagonists; quinoline-4-carboxamides)

IT Tachykinin receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NK3, antagonists; quinoline-4-carboxamides)

IT Mental disorder
(dementia; quinoline-4-carboxamides for treatment of)

IT Bladder
(incontinence; quinoline-4-carboxamides for treatment of)

IT Nerve, disease
(neuropathy; quinoline-4-carboxamides for treatment of)

IT Analgesics

Anticonvulsants
Antiparkinsonian agents
Cognition enhancers
Nervous system agents
(quinoline-4-carboxamides)
IT Alzheimer's disease
(quinoline-4-carboxamides for treatment of)
IT 191796-25-5P 191796-26-6P 191796-27-7P 191796-28-8P 191796-29-9P
191796-30-2P 191796-31-3P 191796-32-4P 191796-33-5P 191796-34-6P
191796-35-7P 191796-36-8P 191796-37-9P 191796-38-0P 191796-39-1P
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191796-45-9P 191796-46-0P 191796-47-1P 191796-48-2P 191796-49-3P
191796-50-6P 191796-51-7P 191796-52-8P 191796-53-9P 191796-54-0P
191796-55-1P 191796-56-2P 191796-57-3P 191796-58-4P 191796-59-5P
191796-60-8P 191796-61-9P 191796-62-0P 191796-63-1P 191796-64-2P
191796-65-3P 191796-66-4P 191796-67-5P 191796-68-6P 191796-69-7P
191796-70-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinoline-4-carboxamides and their use as neurokinin-3 and
neurokinin-2 receptor antagonists)
IT 91-13-4 91-21-4 100-52-7, Benzaldehyde, reactions 103-67-3
105-36-2 108-24-7 108-30-5, reactions 108-31-6, 2,5-Furandione, reactions 110-91-8, Morpholine, reactions 132-60-5 485-89-2
574-98-1 703-59-3, 1H-2-Benzopyran-1,3(4H)-dione 3789-59-1 4385-35-7
5460-29-7 21279-77-6 43071-45-0 52500-61-5 103321-49-9
111524-96-0 111524-97-1 174636-71-6 191796-84-6 191796-85-7
191796-86-8 191796-89-1 191796-90-4 191796-92-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of quinoline-4-carboxamides and their use as neurokinin-3 and
neurokinin-2 receptor antagonists)
IT 88014-09-9P 88014-15-7P 114985-73-8P 117885-67-3P 174636-32-9P
191796-71-1P 191796-72-2P 191796-73-3P 191796-74-4P 191796-75-5P
191796-76-6P 191796-77-7P 191796-78-8P 191796-79-9P 191796-80-2P
191796-81-3P 191796-82-4P 191796-83-5P 191796-87-9P 191796-88-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of quinoline-4-carboxamides and their use as neurokinin-3 and
neurokinin-2 receptor antagonists)

L29 ANSWER 11 OF 11 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 124:232269 MARPAT Full-text
TITLE: Quinoline derivatives as tachykinin NK3 receptor antagonists
INVENTOR(S): Farina, Carlo; Giardina, Giuseppe Arnaldo Mari; Grugni, Mario; Raveglia, Luca Francesco
PATENT ASSIGNEE(S): Smithkline Beecham Farmaceutici S.P.A., Italy
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9532948	A1	19951207	WO 1995-EP2000	19950523
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2191352	AA	19951207	CA 1995-2191352	19950523
CA 2191352	C	20010130		
CA 2257662	AA	19951207	CA 1995-2257662	19950523
AU 9526164	A1	19951221	AU 1995-26164	19950523
AU 699319	B2	19981203		
HU 76286	A2	19970728	HU 1996-3262	19950523
CN 1156451	A	19970806	CN 1995-194338	19950523
CN 1092642	B	20021016		
BR 9507788	A	19970923	BR 1995-7788	19950523
EP 804419	A1	19971105	EP 1995-920894	19950523
EP 804419	B1	20030806		
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JP 10500697	T2	19980120	JP 1996-500287	19950523
RO 114445	B3	19990430	RO 1996-2234	19950523
EP 940391	A2	19990908	EP 1998-204483	19950523
EP 940391	A3	19991110		
EP 940391	B1	20040818		
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JP 2000026314	A2	20000125	JP 1999-172597	19950523
NZ 329979	A	20000728	NZ 1995-329979	19950523
RU 2155754	C2	20000910	RU 1996-124804	19950523
JP 2002179594	A2	20020626	JP 2001-326622	19950523
SK 282721	B6	20021106	SK 1996-1514	19950523
SK 282722	B6	20021106	SK 1999-47	19950523
CZ 291476	B6	20030312	CZ 1996-3470	19950523
AT 246677	E	20030815	AT 1995-920894	19950523
PL 186075	B1	20031031	PL 1995-317381	19950523
PT 804419	T	20031231	PT 1995-920894	19950523
PL 186665	B1	20040227	PL 1995-341889	19950523
ZA 9504269	A	19960514	ZA 1995-4269	19950525
US 5811553	A	19980922	US 1995-450438	19950525
US 6608083	B1	20030819	US 1995-450437	19950525
TW 427977	B	20010401	TW 1995-84105319	19950526
TW 533199	B	20030521	TW 1999-88121625	19950526
BG 64004	B1	20030930	BG 1996-101008	19961125
FI 9604712	A	19970123	FI 1996-4712	19961126
NO 9605036	A	19970124	NO 1996-5036	19961126
CN 1276211	A	20001213	CN 1999-100978	19990115
AU 9912162	A1	19990325	AU 1999-12162	19990119
FI 9900268	A	19990210	FI 1999-268	19990210
NO 9901813	A	19970124	NO 1999-1813	19990416
US 2003236281	A1	20031225	US 2001-867133	20010529
CN 1428145	A	20030709	CN 2002-107941	20020318
PRIORITY APPLN. INFO.:			IT 1994-MI1099	19940527
			IT 1995-MI494	19950314
			AU 1995-26164	19950523

CA 1995-2191352 19950523
EP 1995-920894 19950523
JP 1996-500287 19950523
NZ 1995-287442 19950523
WO 1995-EP2000 19950523
US 1995-450437 19950525

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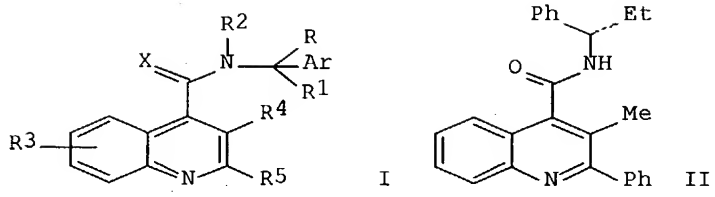


I II

AB NK3 receptor antagonists I [Ar = (un)substituted Ph, naphthyl, cycloalkadienyl, heteroaryl; R = (un)substituted alkyl, cycloalkyl, (un)substituted Ph, phenylalkyl, or heteroaryl, CO2H and derivs., etc.; R1, R2 = H, alkyl; or R1R2 = (CH2)3-5; or RR1 = (CH2)2-5; R3, R4 = H, alkyl, alkenyl, aryl, alkoxy, OH, halo, NO2, amino, etc.; R5 = alkyl, cycloalkyl, (un)substituted (hetero)aryl; X = O, S, N(CN)] are useful in treating pulmonary, CNS, and neurodegenerative disorders, etc. Approx. 115 compds. were prepared For example, amidation of 3-methyl-2- phenylquinoline-4-carbonyl chloride with (R)-α-ethylbenzylamine gave title compound II in 58% yield. II had IC50 of 5.6 nM for displacement of [3H]-senktide from guinea-pig cortical NK3 receptors. Antagonist activity of I was shown by inhibition of senktide-induced contraction of guinea-pig ileum.

IC ICM C07D215-52
ICS A61K031-47; C07D409-04; C07D405-04; C07D401-04; C07D409-12; C07D221-18; C07D417-04; C07D401-12; C07D405-12

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

ST quinolinecarboxamide prepn tachykinin NK3 receptor antagonist

IT Allergy inhibitors
Analgesics
Anticonvulsants and Antiepileptics
Antidepressants
Anxiolytics
Inflammation inhibitors
Nervous system agents
(preparation of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)

IT Antitussives
Hay fever
Kidney, disease
Parkinsonism
Psoriasis
Skin, disease
(treatment; preparation of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)

IT Mental disorder

(Alzheimer's disease, treatment; preparation of quinolinecarboxamide derivs.
as tachykinin NK3 receptor antagonists)
IT Bronchodilators
(antiasthmatics, preparation of quinolinecarboxamide derivs. as tachykinin
NK3 receptor antagonists)
IT Tranquilizers and Neuroleptics
(antipsychotics, preparation of quinolinecarboxamide derivs. as tachykinin
NK3 receptor antagonists)
IT Lung, disease
(chronic obstructive, treatment; preparation of quinolinecarboxamide derivs.
as tachykinin NK3 receptor antagonists)
IT Nervous system
(disease, Huntington's chorea, treatment; preparation of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)
IT Nervous system
(disease, degeneration, treatment; preparation of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)
IT Bladder
(disease, incontinence, treatment; preparation of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)
IT Appetite
(disorder, treatment; preparation of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)
IT Behavior
(disorder, locomotor, treatment; preparation of quinolinecarboxamide derivs.
as tachykinin NK3 receptor antagonists)
IT Eye, disease
(inflammation, treatment; preparation of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)
IT Inflammation
(neurogenic, treatment; preparation of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)
IT Kinin receptors
Receptors
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(tachykinin NK3, preparation of quinolinecarboxamide derivs. as tachykinin
NK3 receptor antagonists)
IT Kinins (animal hormones)
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(tachykinins, preparation of quinolinecarboxamide derivs. as tachykinin NK3
receptor antagonists)
IT 20146-25-2P, 2-(2-Furyl)quinoline-4-carboxylic acid 31792-47-9P, 2-(2-Thienyl)quinoline-4-carboxylic acid 59661-86-8P, 2-Phenylquinoline-4-carboxylic acid chloride 174636-63-6P, 7-Methoxy-2-phenylquinoline-4-carboxylic acid 174636-64-7P, 7-Methoxy-2-phenylquinoline-4-carboxylic acid chloride 174636-65-8P, 7-Hydroxy-2-phenylquinoline-4-carboxylic acid hydroiodide 174636-66-9P, 2-(2-Furyl)quinoline-4-carboxylic acid chloride 174636-67-0P, 2-(4-Pyridyl)quinoline-4-carboxylic acid hydrochloride 174636-68-1P,

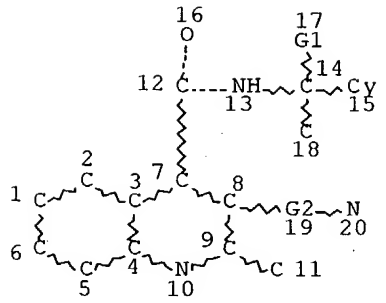
2-(4-Pyridyl)quinoline-4-carboxylic acid chloride hydrochloride
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of quinolinecarboxamide derivs. as tachykinin NK3
receptor antagonists)

IT 174635-48-4P 174635-49-5P 174635-50-8P 174635-51-9P 174635-52-0P
174635-53-1P 174635-54-2P 174635-55-3P 174635-56-4P 174635-57-5P
174635-58-6P 174635-59-7P 174635-60-0P 174635-61-1P 174635-62-2P
174635-63-3P 174635-64-4P 174635-65-5P 174635-66-6P 174635-67-7P
174635-68-8P 174635-69-9P 174635-70-2P 174635-71-3P 174635-72-4P
174635-73-5P 174635-74-6P 174635-75-7P 174635-76-8P 174635-77-9P
174635-78-0P 174635-79-1P 174635-80-4P 174635-81-5P 174635-82-6P
174635-83-7P 174635-84-8P 174635-85-9P 174635-86-0P 174635-87-1P
174635-88-2P 174635-89-3P 174635-90-6P 174635-91-7P 174635-92-8P
174635-93-9P 174635-94-0P 174635-95-1P 174635-96-2P 174635-97-3P
174635-98-4P 174635-99-5P 174636-00-1P 174636-01-2P 174636-02-3P
174636-03-4P 174636-04-5P 174636-05-6P 174636-06-7P 174636-07-8P
174636-08-9P 174636-09-0P 174636-10-3P 174636-11-4P 174636-12-5P
174636-13-6P 174636-14-7P 174636-15-8P 174636-16-9P 174636-17-0P
174636-18-1P 174636-19-2P 174636-20-5P 174636-21-6P 174636-22-7P
174636-23-8P 174636-24-9P 174636-25-0P 174636-26-1P 174636-27-2P
174636-28-3P 174636-29-4P 174636-30-7P 174636-31-8P 174636-32-9P
174636-33-0P 174636-34-1P 174636-35-2P 174636-36-3P 174636-37-4P
174636-38-5P 174636-39-6P 174636-40-9P 174636-41-0P 174636-42-1P
174636-43-2P 174636-44-3P 174636-45-4P 174636-46-5P 174636-47-6P
174636-48-7P 174636-49-8P 174636-50-1P 174636-51-2P 174636-52-3P
174636-53-4P 174636-54-5P 174636-55-6P 174636-56-7P 174636-57-8P
174636-58-9P 174636-59-0P 174636-60-3P 174636-61-4P 174636-62-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)

IT 83-93-2 88-15-3, 2-Acetylthiophene 91-00-9, (Diphenylmethyl)amine 91-56-5, Isatin 98-86-2, Acetophenone, reactions 124-40-3, reactions 132-60-5, 2-Phenylquinoline-4-carboxylic acid 485-89-2 541-88-8, Chloroacetic anhydride 574-98-1, 2-Phthalimidoethyl bromide 585-32-0, α,α-Dimethylbenzylamine 618-36-0, (R,S)-α-Methylbenzylamine 1032-45-7, 8-Hydroxy-2-phenylquinoline-4-carboxylic acid 1122-54-9, 4-Acetylpyridine 1192-62-7, 2-Acetylfuran 2627-86-3, (S)-(-)-α-Methylbenzylamine 2941-19-7, α-(n-Propyl)benzylamine 2941-20-0, α-Ethylbenzylamine 3082-64-2, (R)-α-Ethylbenzylamine 3789-59-1, (S)-α-Ethylbenzylamine 3886-69-9 4364-02-7, 2-(4-Methoxyphenyl)quinoline-4-carboxylic acid 4584-46-7, 2-(Dimethylamino)ethyl chloride hydrochloride 5050-41-9, 2-Pyrrolidinoethyl chloride 5407-04-5 5466-31-9, 2-(p-Chlorophenyl)quinoline-4-carboxylic acid 6633-62-1, 6-Chloro-2-phenylquinoline-4-carboxylic acid 6668-27-5, α-Isopropylbenzylamine 6952-34-7, 2-(4-Hydroxyphenyl)quinoline-4-carboxylic acid 7568-92-5, α-(Hydroxymethyl)benzylamine 15028-39-4, (L)-Methyl phenylglycinate hydrochloride 15028-40-7, (D,L)-Methyl phenylglycinate hydrochloride 17380-74-4, 1-Phenylcyclopentylamine 19883-41-1, (D)-Methyl phenylglycinate hydrochloride 20389-05-3, 2-(4-Methylphenyl)quinoline-4-carboxylic acid 20389-09-7, 2-(2-Chlorophenyl)quinoline-4-carboxylic acid 20389-10-0, 2-(3-Chlorophenyl)quinoline-4-carboxylic acid 21908-20-3,

2-(2-Pyrrolyl)quinoline-4-carboxylic acid 24461-61-8, (R)-Methyl phenylglycinate 25611-78-3, 1-Amino-1,2-diphenylethane 26682-99-5, Methyl phenylglycinate 30081-52-8, 2,3-Diphenylquinoline-4-carbonyl chloride 34698-41-4, 1-Aminoindan 36710-50-6, 3-Amino-5-methyl-2-phenylquinoline-4-carboxylic acid 36735-26-9, 3-Amino-2-phenylquinoline-4-carboxylic acid 37763-23-8, (R)-Methyl (4-hydroxyphenyl)glycinate 40023-89-0, (α-Ethyl-3,4-dichlorobenzyl)amine 43071-45-0, 3-Methyl-2-phenylquinoline-4-carboxylic acid 51586-24-4, α-(Trifluoromethyl)benzylamine 52351-75-4, 6-Methoxyisatin 52500-61-5, 1-Phenyl-2-hydroxypropylamine 57464-25-2, 3-Bromo-2-phenylquinoline-4-carboxylic acid 60289-68-1, 1-(4-Pyridyl)-n-propylamine 61501-03-9, α-n-Butylbenzylamine 74788-15-1, α-n-Heptylbenzylamine 74788-46-8 88831-43-0, (R,S)-Methyl 3-amino-3-phenylpropionate hydrochloride 92566-43-3, 2-(2-Thiazolyl)quinoline-4-carboxylic acid 96669-82-8, 3-Phthalimido-2-phenylquinoline-4-carbonyl chloride 104236-44-4 107635-11-0, Methyl N-methylphenylglycinate 113131-95-6 132289-66-8, (D,L)-Methyl (2-thienyl)glycinate hydrochloride 148887-61-0, 2-(3,4-Dichlorophenyl)quinoline-4-carboxylic acid 174636-69-2, 3-Butyl-2-phenylquinoline-4-carbonyl chloride 174636-70-5, 3-Hexyl-2-phenylquinoline-4-carbonyl chloride 174636-71-6, 3-Methyl-2-phenylquinoline-4-carbonyl chloride 174636-72-7, 2-(2-Methoxyphenyl)quinoline-4-carbonyl chloride 174636-73-8, 2-(2-Fluorophenyl)quinoline-4-carbonyl chloride 174636-74-9, 7-Chloro-2-phenylquinoline-4-carbonyl chloride 174636-75-0, 6-Methyl-2-phenylquinoline-4-carbonyl chloride 174636-76-1, α-(Methoxymethyl)benzylamine 174636-77-2, 6-Chloro-2-phenylquinoline-4-carbonyl chloride 174636-78-3, 3-Ethyl-2-phenylquinoline-4-carbonyl chloride 174636-79-4, 3-n-Propyl-2-phenylquinoline-4-carbonyl chloride 174636-80-7, 6-Bromo-3-methyl-2-(4-bromophenyl)quinoline-4-carbonyl chloride 174636-81-8, 6-Bromo-3-methyl-2-phenylquinoline-4-carbonyl chloride 174636-82-9, 6-Methoxy-2-phenylquinoline-4-carbonyl chloride 174636-83-0, 2-(2-Benzofuryl)quinoline-4-carbonyl chloride 174636-84-1, 2-(3-Thienyl)quinoline-4-carboxylic acid 174636-85-2, 2-(2-Methylphenyl)quinoline-4-carboxylic acid 174636-86-3, 2-(3,4-Methylenedioxyphenyl)quinoline-4-carboxylic acid 174636-87-4, (α-Ethyl-p-methylbenzyl)amine 174636-88-5, 2-(3-Pyrrolyl)quinoline-4-carboxylic acid 174636-89-6, (R)-α-(Phthalimidomethyl)benzylamine 174636-90-9, 3-Chloro-2-phenylquinoline-4-carboxylic acid 174636-91-0, 2-Cyclohexylquinoline-4-carboxylic acid 174636-92-1, 8-Acetoxy-2-phenylquinoline-4-carboxylic acid 174636-93-2, 2-(2,4-Dichlorophenyl)quinoline-4-carboxylic acid 174636-94-3 174636-95-4, 3-Methoxy-2-phenylquinoline-4-carboxylic acid chloride 174636-96-5, 5-Methyl-2-phenylquinoline-4-carboxylic acid 174636-97-6, 1-(2-Thienyl)-n-propylamine hydrochloride 174636-98-7, 3-Methyl-7-methoxy-2-phenylquinoline-4-carbonyl chloride 174636-99-8, 3-Methoxy-5-methyl-2-phenylquinoline-4-carboxylic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)

FILE 'MARPATPREV' ENTERED AT 10:49:30 ON 30 AUG 2004
L27 STR



Ak @21

VAR G1=H/21
REP G2=(1-10) CH2
NODE ATTRIBUTES:
NSPEC IS RC AT 11
NSPEC IS RC AT 18
NSPEC IS RC AT 20
DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 15 21
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

L30 0 SEA FILE=MARPATPREV SSS FUL L27 (MODIFIED ATTRIBUTES)

100.0% PROCESSED 37 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

(FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 10:50:14 ON 30 AUG 2004)
L31 1 S L14

L31 ANSWER 1 OF 1 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2001:330684 BIOSIS Full-text
DOCUMENT NUMBER: PREV200100330684
TITLE: Stepwise modulation of neurokinin-3 and neurokinin-2 receptor affinity and selectivity in quinoline tachykinin receptor antagonists.
AUTHOR(S): Blaney, Frank E.; Raveglia, Luca F.; Artico, Marco; Cavagnera, Stefano; Dartois, Catherine; Farina, Carlo; Grugni, Mario; Gagliardi, Stefania; Luttmann, Mark A.; Martinelli, Marisa; Nadler, Guy M. M. G.; Parini, Carlo; Petrillo, Paola; Sarau, Henry M.; Scheideler, Mark A.; Hay, Douglas W. P.; Giardina, Giuseppe A. M. [Reprint author]
CORPORATE SOURCE: Department of Computational and Structural Sciences, SmithKline Beecham Pharmaceuticals, New Frontiers Science Park, Third Avenue, Harlow, Essex, CM19 5AW, UK giuseppe_giardina@sbphrd.com

SOURCE: Journal of Medicinal Chemistry, (May 24, 2001) Vol. 44, No. 11, pp. 1675-1689. print.
CODEN: JMCMAR. ISSN: 0022-2623.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Jul 2001
Last Updated on STN: 22 Feb 2002

AB A stepwise chemical modification from human neurokinin-3 receptor (hNK-3R)-selective antagonists to potent and combined hNK-3R and hNK-2R antagonists using the same 2-phenylquinoline template is described. Docking studies with 3-D models of the hNK-3 and hNK-2 receptors were used to drive the chemical design and speed up the identification of potent and combined antagonsits at both receptors. (S)-(+)-N-(1-Cyclohexylethyl)-3- ((4-morpholin-4-yl)piperidin-1-yl)methyl-2-phenylquinoline-4-carboxamide (compound 25, SB-400238: hNK-3R binding affinity, Ki = 0.8 nM; hNK-2R binding affinity, Ki = 0.8 nM) emerged as the best example in this approach. Further studies led to the identification of (S)-(+)-N-(1,2,2-trimethylpropyl)-3-((4-piperidin-1-yl)piperidin-1- yl)methyl-2-phenylquinoline-4-carboxamide (compound 28, SB-414240: hNK-3R binding affinity, Ki = 193 nM; hNK-2R binding affinity, Ki = 1.0 nM) as the first hNK-2R-selective antagonist belonging to the 2-phenylquinoline chemical class. Since some members of this chemical series showed a significant binding affinity for the human mu-opioid receptor (hMOR), docking studies were also conducted on a 3-D model of the hMOR, resulting in the identification of a viable chemical strategy to avoid any significant mu-opioid component. Compounds 25 and 28 are therefore suitable pharmacological tools in the tachykinin area to elucidate further the pathophysiological role of NK-3 and NK-2 receptors and the therapeutic potential of selective NK-2 (28) or combined NK-3 and NK-2 (25) receptor antagonists.

FILE 'REGISTRY' ENTERED AT 10:50:42 ON 30 AUG 2004 L32 310 S ?"CARBOXAMIDE HYDROCHLORIDE"?/CNS
L33 66310 S ?METHOXYCARBONYL?/CNS
L34 0 S L32(L)L33

FILE 'CAPLUS' ENTERED AT 10:52:24 ON 30 AUG 2004
L35 29 SEA FILE=CAPLUS ABB=ON PLU=ON (4 CARBOXAMIDE)(S)(PHENYLQUINOLINE OR (PHENYL OR PH)(W)QUINOLINE)
L36 14 SEA FILE=CAPLUS ABB=ON PLU=ON L35(S)(ETHYLBENZYL? OR (ET OR ETHYL)(W)(BZ OR BENZYL?))
L37 1 SEA FILE=CAPLUS ABB=ON PLU=ON L36(S)(METHOXYCARBONYL? OR METHOXY CARBONYL?)

L37 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:674193 CAPLUS Full-text
DOCUMENT NUMBER: 127:355226
TITLE: In vitro and in vivo characterization of NK3 receptors in the rabbit eye by use of selective non-peptide NK3 receptor antagonists
AUTHOR(S): Medhurst, Andrew D.; Hay, Douglas W. P.; Parsons, Andrew A.; Martin, Lenox D.; Griswold, Don E.
CORPORATE SOURCE: Department of Neurosciences Research, SmithKline Beecham Pharmaceuticals, Essex, CM19 5AW, UK
SOURCE: British Journal of Pharmacology (1997), 122(3), 469-476
CODEN: BJPCBM; ISSN: 0007-1188

PUBLISHER: Stockton
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 1 Inhibition of NK3 receptor agonist-induced contraction in the rabbit isolated iris sphincter muscle was used to assess the in vitro functional activity of three 2-phenyl-4-quinolinecarboxamides, members of a novel class of potent and selective non-peptide NK3 receptor antagonists. In addition, an in vivo correlate of this in vitro response, namely NK3 receptor agonist-induced miosis in conscious rabbits, was characterized with some of these antagonists. 2 In vitro senktide (succinyl-[Asp9, MePhe8]-substance P (6-11) and [MePhe7]-neurokinin B[MePhe7]-NKB) were potent contractile agents in the rabbit iris sphincter muscle but exhibited quite different profiles. Senktide produced monophasic log concentration-effect curves with a mean pD2=9.03±0.06 and mean nH=1.2±0.02 (n= 14). In contrast, [MePhe7]-NKB produced shallow log concentration-effect curves which often appeared biphasic (nH=0.54±0.04, n=8), preventing the accurate determination of pD2 values. 3 The contractile responses to the NK3 receptor agonist senktide were antagonized in a surmountable and concentration-dependent manner by SB 223412 [(-)-(S)-N-(α- **ethylbenzyl**)-3-hydroxy-2-**phenylquinoline-4- carboxamide**; 3-30 nM, pA2 = 8.4, slope= 1.8±0.3, n=4], SB 222200 [(-)-(S)-N-(α-**ethylbenzyl**)-3-methyl-2-**phenylquinoline-4-carboxamide**; 30-300 nM, pA2= 7.9, slope= 1.4±0.06, n=4] and SB 218795 [(-)-(R)-N-(α- **methoxycarbonylbenzyl**)-2-**phenylquinoline-4-carboxamide**; 0.3 and 3 μM apparent pKB= 7.4±0.06, n=6]. 4 Contractile responses to the NK3 receptor agonist [MePhe7]-NKB in the rabbit iris sphincter muscle were unaffected by SB 218795 (0.3 and 3 μM, n=8). In contrast, SB 223412 (30 and 300 μM, n=4) and SB 222200 (0.3 and 3 μM, n=4) inhibited responses to low concns. (≤ 1 nM), to a greater extent than higher concns. (>1 nM) of [MePhe7]-NKB. Furthermore, log concentration-effect curves to [MePhe7]-NKB became steeper and monophasic in the presence of each antagonist. 5 SB 218795 (3 μM, n=4) had no effect on contractions induced by transmural nerve stimulation (2 Hz) or substance P, exemplifying the selectivity of this class of antagonist for functional NK3 receptors over NK1 receptors in the rabbit. 6 In vivo, senktide (1, 10 and 25 μg i.v.,i.e. 1.2, 11.9 and 29.7 nmol, resp.) induced concentration-dependent bilateral miosis in conscious rabbits (maximum pupillary constriction =4.25±0.25 mm; basal pupillary diameter 7.75±0.48 mm; n=4). The onset of miosis was within 2-5 min of application of senktide and responses lasted up to 30 min. Responses to two i.v. administrations of 25 μg senktide given 30 min apart revealed no evidence of tachyphylaxis. Topical administration of atropine (1%) to the eye enhanced pupillary responses to 25 μg senktide. This was probably due to the mydriatic effect of atropine since it significantly increased baseline pupillary diameter from 7.0±0.4 mm to 9.0±0.7 mm (n=4), thereby increasing the maximum capacity for miosis. Senktide-induced miosis was inhibited by SB 222200 (1 and 2 mg kg-1, i.v., i.e. 2.63 and 5.26 μmol kg-1; maximum inhibition 100%; n=3-4), SB 223412 (0.5 and 1 mg kg-1, i.v., i.e. 1.31 and 2.61 μmol kg-1; maximum inhibition 100%; n=3), SB 218795 (0.5 and 1 mg kg-1, i.v., i.e. 1.26 and 2.52 μmol kg-1; maximum inhibition 78%; n=3), and the structurally distinct NK3 receptor antagonist SR 142801 [(S)-(N)-(1-(3-(1-benzoyl-3-(3,4-dichlorophenyl)piperidin-3-yl)propyl)-4-phenylpipiperidin-4-yl)-N-methylacetamide; 1.5 mg kg-1, i.v.,i.e. 2.47 μmol kg-1, maximum inhibition 92%; n=3]. Opical administration of senktide (25 μg; 29.7 nmol) to the eye induced unilateral miosis in the treated eye only. At this dose there was no significant difference (P<0.05) between pupillary constriction obtained by topical or i.v. senktide, and topically administered atropine had no

significant effect on responses to topical senktide (n=4). 8 [MePhe7]-NKB (125, 250 and 500 μg, i.v., i.e. 98.31, 196.62 and 393.24 nmol, resp.) also induced bilateral miosis in conscious rabbits (maximum pupillary constriction=4.13±0.30 mm; n=4), but in contrast to in vitro studies this agonist was approx. 100 fold less potent than senktide. [MePhe7]-NKB-induced miosis was inhibited by SB 222200 (5 mg kg-1, i.v., i.e. 13.14 μmol kg-1; maximum inhibition 69%; n=3). 9 In summary, SB 223412, SB 222200 and SB 218795 are potent and selective antagonists of NK3 receptor-mediated contraction in the rabbit isolated iris sphincter muscle. In addition, NK3 receptor agonist-induced miosis in conscious rabbits is a good in vivo correlate of the in vitro rabbit iris sphincter muscle preparation and appears to be a useful model for characterizing the pharmacodynamic profile and efficacy of structurally distinct NK3 receptor antagonists, such as SB 222200, SB 223412, SB 218795 and SR 142801.

IT Tachykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NK3; characterization of NK3 receptors in the rabbit eye by use of selective non-peptide NK3 receptor antagonists)

IT Miosis
(characterization of NK3 receptors in the rabbit eye by use of selective non-peptide NK3 receptor antagonists)

IT Eye
Eye
(iris sphincter; characterization of NK3 receptors in the rabbit eye by use of selective non-peptide NK3 receptor antagonists)

IT 173050-51-6, SR 142801 174635-53-1, SB 218795 174635-69-9, SB 222200 174636-32-9, SB 223412
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(characterization of NK3 receptors in the rabbit eye by use of selective non-peptide NK3 receptor antagonists)

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

(FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 11:00:38 ON 30 AUG 2004)
L38 1 S L37

L38 ANSWER 1 OF 1 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 1997:506151 BIOSIS Full-text
DOCUMENT NUMBER: PREV199799805354
TITLE: In vitro and in vivo characterization of NK-3 receptors in the rabbit eye by use of selective non-peptide NK-3 receptor antagonists.
AUTHOR(S): Medhurst, Andrew D. [Reprint author]; Hay, Douglas W. P.; Parsons, Andrew A.; Martin, Lenox D.; Griswold, Don E.
CORPORATE SOURCE: Dep. Neurosciences Res., SmithKline Beecham Pharmaceuticals, Third Avenue, Harlow, Essex CM19 5AW, UK
SOURCE: British Journal of Pharmacology, (1997) Vol. 122, No. 3, pp. 469-476.
CODEN: BJPCBM. ISSN: 0007-1188.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Nov 1997
Last Updated on STN: 27 Jan 1998

AB 1. Inhibition of NK-3 receptor agonist-induced contraction in the rabbit isolated iris sphincter muscle was used to assess the in vitro functional activity of three 2-phenyl-4-quinolinecarboxamides, members of a novel

class of potent and selective non-peptide NK-3 receptor antagonists. In addition, an in vivo correlate of this in vitro response, namely NK-3 receptor agonist-induced miosis in conscious rabbits, was characterized with some of these antagonists. 2. In vitro senktide (succinyl-(Asp-9,MePhe-8)-substance P (6-11) and (MePhe-7)-neurokinin B ((MePhe-7)NKB) were potent contractile agents in the rabbit iris sphincter muscle but exhibited quite different profiles. Senktide produced monophasic log concentration-effect curves with a mean pD-2 = 9.03 +- 0.06 and mean n-H = 1.2 +- 0.02 (n = 14). In contrast, (MePhe-7)-NKB produced shallow log concentration-effect curves which often appeared biphasic (n-H = 0.54 +- 0.04, n = 8), preventing the accurate determination of pD-2 values. 3. The contractile responses to the NK-3 receptor agonist senktide were antagonized in a surmountable and concentration-dependent manner by SB 223412 ((-)-(S)-N-(alpha-**ethylbenzyl**)-3-hydroxy-2- **phenylquinoline-4-carboxamide**; 3 - 30 nM, pA-2 = 8.4, slope = 1.8 +- 0.3, n = 4), SB 222200 ((-)-(S)-N-(alpha- **ethylbenzyl**)-3-methyl-2-**phenylquinoline-4- carboxamide**; 30 - 300 nM, pA-2 = 7.9, slope = 1.4 +- 0.06, n = 4) and SB 218795 ((-)-(R)-N-(alpha-**methoxycarbonylbenzyl**)-2- **phenylquinoline-4-carboxamide**; 0.3 and 3 mu-M apparent pK-B = 7.4 +- 0.06, n = 6). 4. Contractile responses to the NK-3 receptor agonist (MePhe-7)-NKB in the rabbit iris sphincter muscle were unaffected by SB 218795 (0.3 and 3 mu-M, n=8). In contrast, SB 223412 (30 and 300 mu-M, n=4) and SB 222200 (0.3 and 3 mu-M, n = 4) inhibited responses to low concentrations (ltoreq 1 nM), to a greater extent than higher concentrations (gt 1 nM) of (MePhe-7)-NKB. Furthermore, log concentration-effect curves to (MePhe-7)-NKB became steeper and monophasic in the presence of each antagonist. 5. SB 218795 (3 mu-M, n=4) had no effect on contractions induced by transmural nerve stimulation (2 Hz) or substance P, exemplifying the selectivity of this class of antagonist for functional NK-3 receptors over NK-1 receptors in the rabbit. 6. In vivo, senktide (1, 10 and 25 mu-g i.v., i.e. 1.2, 11.9 and 29.7 nmol, respectively) induced concentration-dependent bilateral miosis in conscious rabbits (maximum pupillary constriction = 4.25 +- 0.25 mm; basal pupillary diameter 7.75 +- 0.48 mm; n = 4). The onset of miosis was within 2 - 5 min of application of senktide and responses lasted up to 30 min. Responses to two i.v. administrations of 25 mu-g senktide given 30 min apart revealed no evidence of tachyphylaxis. Topical administration of atropine (1%) to the eye enhanced pupillary responses to 25 mu-g senktide. This was probably due to the mydriatic effect of atropine since it significantly increased baseline pupillary diameter from 7.0 +- 0.4 mm to 9.0 +- 0.7 mm (n = 4), thereby increasing the maximum capacity for miosis. Senktide-induced miosis was inhibited by SB 222200 (1 and 2 mg kg-1, i.v., i.e. 2.63 and 5.26 mu-mol kg-1; inhibition 100%; n=3-4), SB 223412 (0.5 and 1 mg kg-1, i.v., i.e. 1.31 and 2.61 mu-mol kg-1; maximum inhibition 100%; n=3), SB 218795 (0.5 and 1 mg kg-1, i.v., i.e. 1.26 and 2.5 mu-mol kg-1; maximum inhibition 78%; n = 3), and the structurally distinct NK-3 receptor antagonist SR 142801 ((S)-(N)-(1-3-1-benzoyl-3-(3,4-dichlorophenyl)piperidin-3-yl)propyl)- 4-phenylepiperidin-4-yl)-N-methylacetamide; 1.5 mg kg-1, i.v., i.e. 2.47 mu-mol kg-1, maximum inhibition 92%; n = 3). 7. Topical administration of senktide (25 mu-g; 29.7 nmol) to the eye induced unilateral miosis in the treated eye only. At this dose there was no significant difference (P lt 0.05) between pupillary constriction obtained by topical or i.v. senktide, and topically administered atropine had no significant effect on responses to topical senktide (n = 4). 8. (MePhe-7)-NKB (125, 250 and 500 mu-g, i.v., i.e. 98.31, 196.62 and 393.24 nmol, respectively) also induced bilateral miosis in conscious rabbits (maximum pupillary constriction = 4.13 +- 0.30 mm; n = 4), but in contrast to in vitro studies this agonist was approximately 100 fold less potent than senktide. (MePhe-7)-NKB-induced miosis was inhibited

by SB 222200 (5 mg kg-1, i.v., i.e. 13.14 mu-mol kg-1; maximum inhibition 69%; n=3). 9. In summary, SB 223412, SB 222200 and SB 218795 are potent and selective antagonists of NK-3 receptor-mediated contraction in the rabbit isolated iris sphincter muscle. In addition, NK-3 receptor agonist-induced miosis in conscious rabbits is a good in vivo correlate of the in vitro rabbit iris sphincter muscle preparation and appears to be a useful model for characterizing the pharmacodynamic profile and efficacy of structurally distinct NK-3 receptor antagonists, such as SB 222200, SB 223412, SB 218795 and SR 142801.

FILE 'USPATFULL' ENTERED AT 11:14:31 ON 30 AUG 2004 L39 6 S L37

L39 ANSWER 1 OF 6 USPATFULL on STN

ACCESSION NUMBER:	2004:152247 USPATFULL Full-text
TITLE:	Quinoline-4-carboxamide derivatives as NK-2 and NK-3 receptor antagonists
INVENTOR(S):	Giardina, Giuseppe Arnaldo Maria, Milan, ITALY Grugni, Mario, Domodossola, ITALY Graziani, Davide, Milan, ITALY Raveglia, Luca Francesco, Milan, ITALY
PATENT ASSIGNEE(S):	SmithKline Beecham SpA (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004116469	A1	20040617
APPLICATION INFO.:	US 2003-721644	A1	20031125 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2002-52925, filed on 16 Jan 2002, ABANDONED Continuation of Ser. No. US 1999-424122, filed on 17 Nov 1999, ABANDONED A 371 of International Ser. No. WO 1998-EP3014, filed on 18 May 1998, UNKNOWN

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1997-10750	19970523
	IT 1997-MI2354	19971017
	IT 1997-MI2775	19971216

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	SMITHKLINE BEECHAM CORPORATION, Corporate Intellectual Property - UW2220, P.O. Box 1539, King of Prussia, PA, 19406-0939
NUMBER OF CLAIMS:	19
EXEMPLARY CLAIM:	1
LINE COUNT:	1814

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A compound, or a solvate or a salt thereof, of formula (I): wherein, Ar is an optionally substituted aryl or a C.sub.5-7 cycloalkdienyl group, or a C.sub.5-7 cycloalkyl group or an optionally substituted single or fused ring aromatic heterocyclic group; R is C.sub.1-6 alkyl, C.sub.3-7 cycloalkyl, C.sub.3-7 cycloalkylalkyl, optionally substituted phenyl or phenyl C.sub.1-6 alkyl, an optionally substituted five-membered heteroaromatic ring comprising up to four heteroatoms selected from O and N, hydroxy C.sub.1-6 alkyl, amino C.sub.1-6 alkyl, C.sub.1-6 alkylaminoalkyl, di C.sub.1-6 alkylaminoalkyl, C.sub.1-6 acylaminoalkyl, C.sub.1-6 alkoxyalkyl, C.sub.1-6 alkylcarbonyl, carboxy, C.sub.1-6 alkoxycarbonyl, C.sub.1-6 alkoxycarbonyl C.sub.1-6 alkyl, aminocarbonyl,

C.sub.1-6 alkylaminocarbonyl, di C.sub.1-6 alkylaminocarbonyl, halogeno C.sub.1-6 alkyl; or R is a group --(CH.sub.2).sub.p-- wherein p is 2 or 3 which group forms a ring with a carbon atom of Ar, R.sub.1 represents hydrogen or up to four optional substituents selected from the list consisting of: C.sub.1-6 alkyl, C.sub.1-6 alkenyl, aryl, C.sub.1-6 alkoxy, hydroxy, halogen, nitro, cyano, carboxy, carboxamido, sulphonamido, C.sub.1-6 alkoxycarbonyl, trifluoromethyl, acyloxy, phthalimido, amino or mono- and di-C.sub.1-6 alkylamino; R.sub.2 represents a moiety --(CH.sub.2).sub.n--NY.sub.1Y.sub.2 wherein n is an integer in the range of from 1 to 9, Y.sub.1 and Y.sub.2 are independently selected from hydrogen; C.sub.1-6-alkyl; C.sub.1-6 alkyl substituted with hydroxy, C.sub.1-6 alkylamino or bis (C.sub.1-6 alkyl) amino; C.sub.1-6-alkenyl; aryl or aryl-C.sub.1-6-alkyl or Y.sub.1 and Y.sub.2 together with the nitrogen atom to which they are attached represent an optionally substituted N-linked single or fused ring heterocyclic group; R.sub.3 is branched or linear C.sub.1-6 alkyl, C.sub.3-7 cycloalkyl, C.sub.4-7 cycloalkylalkyl, optionally substituted aryl, or an optionally substituted single of fuse ring aromatic heterocyclic group; and R.sub.4 represents hydrogen or C.sub.1-6 alkyl; a pharmaceutical composition comprising such a compound, process for preparing such a compound and the use of such a compound in medicine. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L39 ANSWER 2 OF 6 USPATFULL on STN

ACCESSION NUMBER:	2004:7895 USPATFULL Full-text		
TITLE:	Combination treatment for depression and anxiety		
INVENTOR(S):	Sobolov-Jaynes, Susan B., Ivoryton, CT, UNITED STATES Lowe, John A., III, Stonington, CT, UNITED STATES McLean, Stafford, Stonington, CT, UNITED STATES		
PATENT ASSIGNEE(S):	Pfizer Inc. (U.S. corporation)		

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004006135	A1	20040108	
APPLICATION INFO.:	US 2003-386582	A1	20030312	(10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-389975P	20020619 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	PFIZER INC, 150 EAST 42ND STREET, 5TH FLOOR - STOP 49, NEW YORK, NY, 10017-5612
NUMBER OF CLAIMS:	35
EXEMPLARY CLAIM:	1
LINE COUNT:	6820

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to a method of treating depression or anxiety in a mammal, including a human, by administering to the mammal a CNS-penetrant NK-1 receptor antagonist (e.g., a substance P receptor antagonist) in combination with an NK-3 antagonist agent. It also relates to pharmaceutical compositions containing a pharmaceutically acceptable carrier, a CNS-penetrant NK-1 receptor antagonist and an NK-3 antagonist.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L39 ANSWER 3 OF 6 USPATFULL on STN

ACCESSION NUMBER:	2003:335403 USPATFULL Full-text
TITLE:	Quinoline derivatives(2)
INVENTOR(S):	Farina, Carlo, Milan, ITALY Maria Giardina, Giuseppe Arnaldo, Milan, ITALY Grugni, Mario, Domodossola, ITALY Raveglia, Luca Francesco, Milan, ITALY

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003236281	A1	20031225
APPLICATION INFO.:	US 2001-867133	A1	20010529 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 1995-450437, filed on 25 May 1995, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	IT 1994-MI1099	19940527
	IT 1995-MI494	19950314

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	GLAXOSMITHKLINE, Corporate Intellectual Property - UW2220, P. O. Box 1539, King of Prussia, PA, 19406-0939
NUMBER OF CLAIMS:	12
EXEMPLARY CLAIM:	1
LINE COUNT:	2882

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB NK.sub.3 receptor antagonists of formula (I): ##STR1##

are useful in treating inter alia pulmonary disorders, CNS disorders and neurodegenerative disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L39 ANSWER 4 OF 6 USPATFULL on STN

ACCESSION NUMBER:	2003:4143 USPATFULL Full-text
TITLE:	Quinoline-4-carboxamide derivatives as NK-2 and NK-3 receptor antagonists
INVENTOR(S):	Giardina, Giuseppe Arnaldo Maria, Milan, ITALY Grugni, Mario, Domodossola, ITALY Graziani, Davide, Milan, ITALY Raveglia, Luca Francesco, Milan, ITALY

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003004183	A1	20030102
APPLICATION INFO.:	US 2002-52925	A1	20020116 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2000-731190, filed on 6 Dec 2000, PENDING Continuation of Ser. No. US 1999-424122, filed on 17 Nov 1999, ABANDONED A 371 of International Ser. No. WO 1998-EP3014, filed on 18 May 1998, UNKNOWN

	NUMBER	DATE

PRIORITY INFORMATION: GB 1997-10750 19970523
IT 1997-MI2354 19971017
IT 1997-MI2775 19971216
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: SMITHKLINE BEECHAM CORPORATION, Corporate Intellectual Property - UW2220, P.O. Box 1539, King of Prussia, PA, 19406-0939
NUMBER OF CLAIMS: 19
EXEMPLARY CLAIM: 1
LINE COUNT: 1805
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A compound, or a solvate or a salt thereof of formula (I), wherein, Ar is an optionally substituted aryl or a C.sub.5-7cycloalkdienyl group, or a C.sub.5-7cycloalkyl group or an optionally substituted single or fused ring aromatic heterocyclic group; R is C.sub.1-6alkyl, C.sub.3-7cycloalkyl, C.sub.3-7cycloalkylalkyl, optionally substituted phenyl or phenylC.sub.1-6alkyl, an optionally substituted five-membered heteroaromatic ring comprising up to four heteroatoms selected from O and N, hydroxy C.sub.1-6alkyl, amino C.sub.1-6 alkyl, C.sub.1-6alkylaminoalkyl, di C.sub.1-6alkylaminoalkyl, C.sub.1-6acylaminoalkyl, C.sub.1-6alkoxyalkyl, C.sub.1-6alkylcarbonyl, carboxy, C.sub.1-6alkoxycarbonyl, C.sub.1-6alkoxycarbonylC.sub.1-6alkyl, aminocarbonyl, C.sub.1-6alkylaminocarbonyl, di C.sub.1- 6alkylaminocarbonyl, halogenoC.sub.1-6alkyl; or R is a group --(CH.sub.2)p-- wherein p is 2 or 3 which group forms a ring with a carbon atom of Ar; R.sub.1 represents hydrogen or up to four optional substituents selected from the list consisting of, C.sub.1-6alkyl, C.sub.1-6alkenyl, aryl, C.sub.1-6alkoxy, hydroxy, halogen, nitro, cyano, carboxy, carboxamido, suphonamido, C.sub.1-6alkoxycarbonyl, trifluoromethyl, acyloxy, phthalimido, amino or mono- and di-C.sub.1-6alkylamino; R.sub.2 represents a moiety --(CH.sub.2).sub.n-- NY.sub.1Y.sub.2, wherein n is an integer in the range of 1 to 9, Y.sub.1 and Y.sub.2 are independently selected from hydrogen, C.sub.1-6alkyl, C.sub.1-6alkyl substituted with hydroxy, C.sub.1-6alkylamino or bis (C.sub.1-6alkyl)amino, C.sub.1-6alkyl or Y.sub.1 and Y.sub.2 together with the nitrogen atom to which they are attached represent an optionally substituted N-linked single or fused ring heterocyclic group; R.sub.3 is branched or linear C.sub.1-6alkyl, C.sub.3-7cycloalkyl, C.sub.4-7cycloalkylalkyl, optionally substituted aryl, or an optionally substituted single or fused ring aromatic heterocyclic group; and R.sub.4 represents hydrogen or C.sub.1-6 alkyl; a pharmaceutical composition comprising such a compound, process for preparing such a compound and the use of such a compound in medicine.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L39 ANSWER 5 OF 6 USPATFULL on STN
ACCESSION NUMBER: 2001:136665 USPATFULL Full-text
TITLE: Quinoline derivatives
INVENTOR(S): Giardina, Giuseppe Arnaldo Maria, Milan, Italy
Grugni, Mario, Verbania, Italy
Raveglia, Luca Francesco, Milan, Italy
Farina, Carlo, Milan, Italy
PATENT ASSIGNEE(S): SmithKline Beecham S.p.A., Milan, Italy (non-U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION:	US 6277862	B1	20010821
	WO 9721680		19970619
APPLICATION INFO.:	US 1998-77151		19980522 (9)
	WO 1996-EP5203		19961122
			19980522 PCT 371 date
			19980522 PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	IT 1995-MI2461	19951124
	IT 1996-MI1689	19960802

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Seaman, D. Margaret
LEGAL REPRESENTATIVE: Stein-Fernandez, Nora, Venetianer, Stephen, Kinzig, Charles M.
NUMBER OF CLAIMS: 29
EXEMPLARY CLAIM: 1
LINE COUNT: 2231
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A compound, or a solvate or a salt thereof, of formula (I), wherein, Ar is an optionally substituted aryl or a C.sub.5-7 cycloalkdienyl group, or an optionally substituted single or fused ring aromatic heterocyclic group; R, R.sub.1, R.sub.2 and R.sub.3 are as defined in the description; a process for the preparation of such a compound, a pharmaceutical composition containing such a compound or composition in medicine. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L39 ANSWER 6 OF 6 USPATFULL on STN
ACCESSION NUMBER: 2001:128858 USPATFULL Full-text
TITLE: Quinoline-4-carboxamide derivatives as NK-2 and NK-3 receptor antagonists
INVENTOR(S): Glardina, Giuseppe Arnaldo Maria, Milan, Italy
Grugni, Mario, Domodossola, Italy
Graziani, Davide, Milan, Italy
Raveglia, Luca Francesco, Milan, Italy

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2001012846	A1	20010809
APPLICATION INFO.:	US 2000-731190	A1	20001206 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1999-424122, filed on 17 Nov 1999, ABANDONED A 371 of International Ser. No. WO 1998-EP3014, filed on 18 May 1998, UNKNOWN

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1997-10750	19970523
	IT 1997-MI2354	19971017
	IT 1997-MI2775	19971216

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: SMITHKLINE BEECHAM CORPORATION, Corporate Intellectual Property - UW2220, P.O. Box 1539, King of Prussia, PA,

19406-0939
NUMBER OF CLAIMS: 19
EXEMPLARY CLAIM: 1
LINE COUNT: 2048
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A compound, or a solvate or a salt thereof of formula (I), wherein, Ar is an optionally substituted aryl or a C.sub.5-7cycloalkdienyl group; or a C.sub.5-7cycloalkyl group or an optionally substituted single or fused ring aromatic heterocyclic group; R is C.sub.1-6 alkyl, C.sub.3-7cycloalkyl, C.sub.3-7cycloalkylalkyl, optionally substituted phenyl or phenylC.sub.1-6alkyl, an optionally substituted five-membered heteroaromatic ring comprising up to four heteroatoms selected from O and N, hydroxyC.sub.1-6alkyl, amino C.sub.1-6 alkyl, C.sub.1-6alkylaminoalkyl, di C.sub.1-6alkylaminoalkyl, C.sub.1-6acylaminoalkyl, C.sub.1-6alkoxyalkyl, C.sub.1-6alkylcarbonyl, carboxy, C.sub.1-6alkoxycarbonyl, C.sub.1-6alkoxycarbonylC.sub.1-6alkyl, aminocarbonyl, C.sub.1-6alkylaminocarbonyl, di C.sub.1- 6alkylaminocarbonyl, halogenoC.sub.1-6alkyl; or R is a group --(CH.sub.2)p-- wherein p is 2 or 3 which group forms a ring with a carbon atom of Ar; R.sub.1 represents hydrogen or up to four optional substituents selected from the list consisting of, C.sub.1-6alkyl, C.sub.1-6alkenyl, aryl, C.sub.1-6alkoxy, hydroxy, halogen, nitro, cyano, carboxy, carboxamido, suphonamido, C.sub.1-6 alkoxycarbonyl, trifluoromethyl, acyloxy, phthalimido, amino or mono- and di-C.sub.1-6alkylamino; R.sub.2 represents a moiety --(CH.sub.2).sub.n-- NY.sub.1Y.sub.2, wherein n is an integer in the range of 1 to 9, Y.sub.1 and Y.sub.2 are independently selected from hydrogen, C.sub.1-6alkyl, C.sub.1-6alkyl substituted with hydroxy, C.sub.1-6 alkylamino or bis (C.sub.1-6alkyl)amino, C.sub.1-6alkyl or Y.sub.1 and Y.sub.2 together with the nitrogen atom to which they are attached represent an optionally substituted N-linked single or fused ring heterocyclic group; R.sub.3 is branched or linear C.sub.1-6alkyl, C.sub.3-7cycloalkyl, C.sub.4-7cycloalkylalkyl, optionally substituted aryl, or an optionally substituted single or fused ring aromatic heterocyclic group; and R.sub.4 represents hydrogen or C.sub.1-6 alkyl; a pharmaceutical composition comprising such a compound, process for preparing such a compound and the use of such a compound in medicine.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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